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United States Patent [19]

Tower

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[45] Date of Patent: Feb. 14, 1995

[54] IMPERMEABLE EXPANDABLE INTRAVASCULAR STENT

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[73] Assignee: Numed, Inc., Nicholville, N.Y.

[21] Appl. No.: 145,435

[22] Filed: Oct. 29, 1993

[51] Int. Cl.[6] A61M 29/00

[52] U.S. Cl. 606/198; 623/1; 623/12

[58] Field of Search 606/198, 200, 108, 191-194; 623/1, 12

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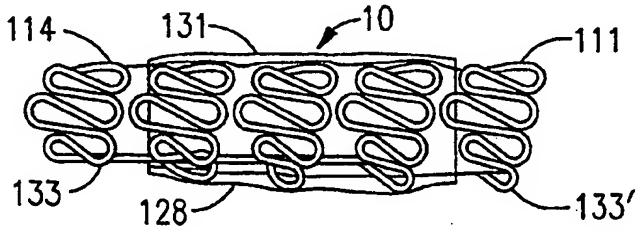
Primary Examiner—Stephen C. Pellegrino
Assistant Examiner—William W. Lewis
Attorney, Agent, or Firm—Harris Beach & Wilcox

[57] ABSTRACT

There is disclosed a radially expandable stent for intravascular implantation comprising a distensible frame and an impermeable deformable membrane interconnecting portions of the frame to form an impermeable exterior wall. The membrane is formed of a synthetic non-latex, non-vinyl polymer, and the frame comprises a fine wire of annealed platinum. The comprises a plurality of helically aligned circumferential sections including two end sections and a plurality of intermediate sections that define a cylinder having a longitudinal axis, the cylinder being formed of a continuous wire with the circumferential sections being spaced along the axis in abutting contact. Each of the circumferential sections have expandable segments that impart radial expandability to the sections. The expandable segments are tear-drop shaped elements that are alternately inverted about the circumferential sections, each element containing a base and a pair of legs that come together at a common apex when the stent is in an unexpanded condition. One of the end sections has a pigtail that is passed back along the circumferential sections and is joined to the other end section to prevent axial expansion of the expanded during radial expansion.

5 Claims, 2 Drawing Sheets



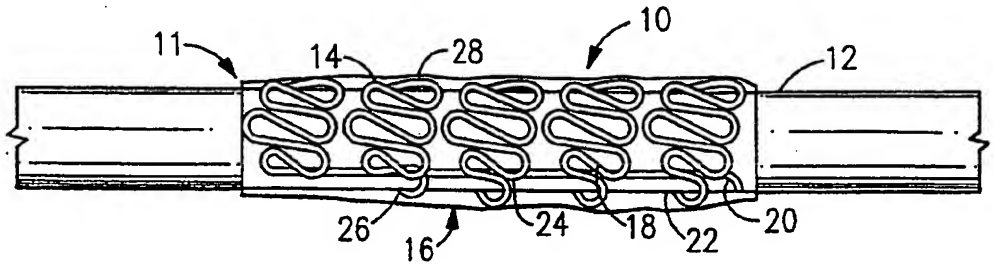


FIG.1

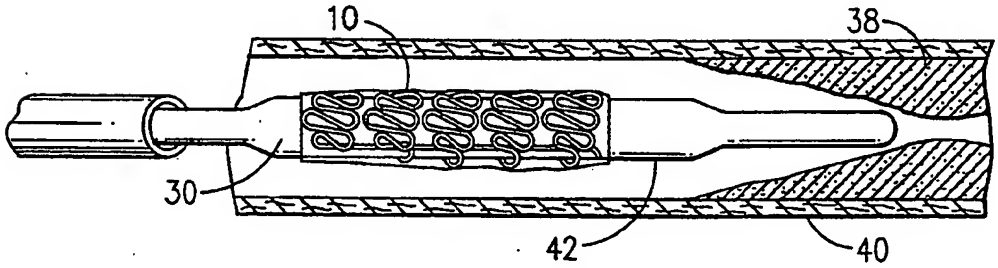


FIG.2

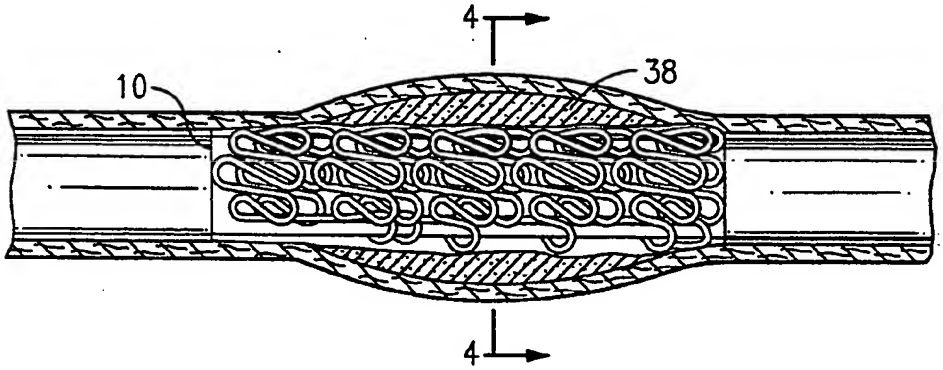


FIG.3

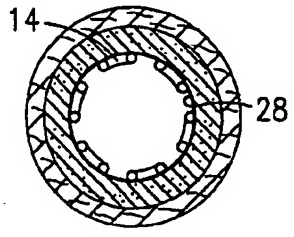


FIG.4

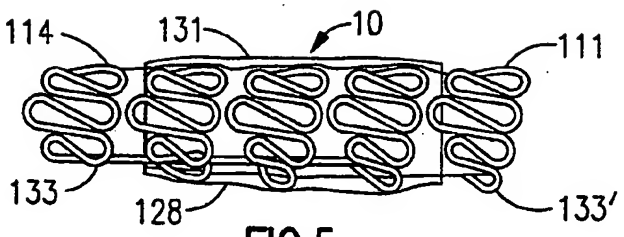


FIG.5

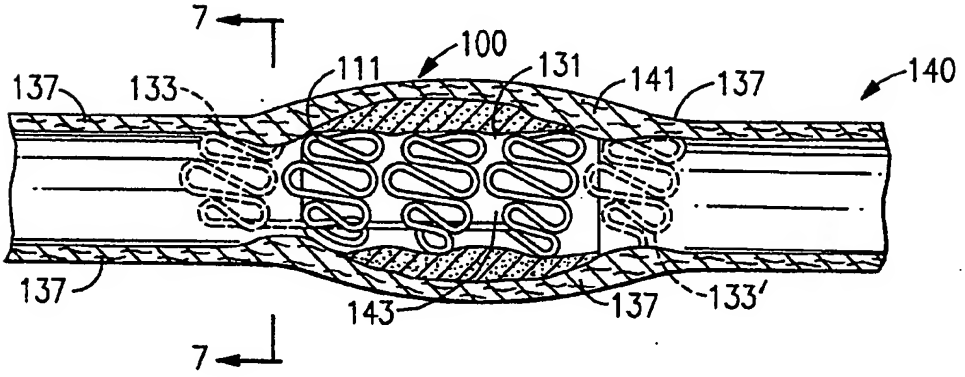
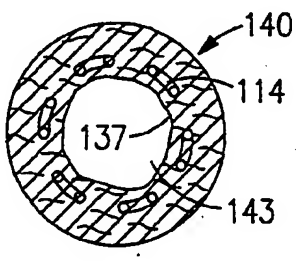


FIG.6

FIG.7



IMPERMEABLE EXPANDABLE INTRAVASCULAR STENT

BACKGROUND OF THE INVENTION

1. Field of the Invention

This invention relates to intravascular implants for maintaining vascular patency in human blood vessels. More particularly, this invention relates to a radially expandable stent made from a fine wire formed into a serpentine ribbon wound into a cylindrical shape for introduction into a body vessel for balloon expansion therein in a radial fashion to support the wall of the vessel when in the expanded configuration. The stent includes an impermeable membrane that lies in the plane of the cylinder. This invention is particularly useful in transluminal implantation of a stent for use in the coronary angioplasty to prevent restenosis, and for the treatment of aneurysms or subintimal dissections.

2. Description of the Prior Art

The basic concept of stents has been known for a number of years. Various types of stents have been proposed and patented, including self-expanding spring types, compressed spring types, mechanically actuated expandable devices, heat actuated expandable devices, and the like. More recently, expandable sleeves have been proposed such as shown in Palmaz, U.S. Pat. No. 4,733,665. In this disclosure there is shown a sleeve having slots therethrough to form a permeable mesh. The sleeve is placed transluminally, and then expanded by a balloon catheter through the elastic limit of the metal so as to permanently deform the sleeve into supporting contact with the interior surface of a blood vessel. Other examples of expandable wire stents are shown in Hillstead, U.S. Pat. No. 4,865,516, and Wiktor, U.S. Pat. No. 4,886,062.

In my U.S. Pat. No. 5,217,483 (referred to hereinafter as the '483 Patent) I disclose the use of a fine platinum wire bent into a serpentine flat ribbon which is wound around a mandrel into a radially expandable cylindrical sleeve for mounting on a balloon catheter for transluminal intravascular placement. The expanded sleeve as disposed in a vessel possesses gaps or interstices which are believed to protect the vascular endothelium from contact therewith, and to promote endothelial proliferation and remodeling of the vascular intima about the sleeve. However in many cases the trauma of implantation causes microscopic or even macroscopic intimal tears, and exposes the subintimal space to the bloodstream. This is undesirable as further dissection of the vessel is possible. Furthermore tissue reactions, including thrombus formation, intimal fibroplasia, and cicatrization could result in restenosis of the vessel.

Permeable transluminally placed intravascular stents are suboptimum for the treatment of aneurysms. While the structure of the expanded mesh may reduce the pulsatile forces acting against a weakened arterial wall, this effect is doubtless incomplete. The art has long utilized grossly impermeable continuous structures such as Teflon grafts and implants for aneurysm repair in larger vessels by conventional open surgical techniques.

SUMMARY OF THE INVENTION

It is an object of the present invention to provide an improved expandable stent adapted to percutaneous intravascular implantation for supporting the wall of a blood vessel and for stabilizing an aneurysm thereof.

It is another object of the present invention to provide an improved intravascular stent that reduces the rate of restenosis in a vessel subjected to angioplasty therewith.

It is yet another object of the present invention to provide an improved expandable stent that can be percutaneously implanted in a vessel without injury to the vessel.

These and other objects of the present invention are attained by a radially expandable stent for intravascular implantation comprising a distensible frame and an impermeable deformable membrane interconnecting portions of the frame to form an impermeable exterior wall. The tubular member is dimensioned to receive an inflatable catheter for intravascular placement and radial expansion therewith. Expansion of the catheter and the stent brings the wall surface into supporting contact with an interior surface of a vessel.

The membrane is formed of a synthetic non-latex, non-vinyl polymer, and the frame comprises a fine wire of annealed platinum.

According to one aspect of the invention, the membrane extends from end to end of the frame.

In another aspect of the invention the membrane is disposed on the central portion of the frame, and at least one of the frame ends are not covered by or in contact with the membrane in order to permit anchoring of the ends to the vessel once tissue reaction or remodeling of the vessel wall has occurred about the ends of the stent.

In a preferred embodiment the radially expandable stent comprises a plurality of helically aligned circumferential sections including two end sections and a plurality of intermediate sections that define a cylinder having a longitudinal axis, the cylinder being formed of a continuous wire with the circumferential sections being spaced along the axis in abutting contact. Each of the circumferential sections have expandable segments that impart radial expandability to the sections, whereby the sections have an unexpanded insertion circumference and an expanded implantation circumference that is greater than the insertion circumference. The expandable segments are tear-drop shaped elements that are alternately inverted about the circumferential sections, each element containing a base and a pair of legs that come together at a common apex when the stent is in an unexpanded condition. One of the end sections has a free end or pigtail that is passed back along the circumferential sections and is joined to the other end section to prevent axial expansion of the stent during radial expansion. The elements and the circumferential segments are interconnected by a distensible impermeable membrane formed of a synthetic non-latex, non-vinyl polymer to define a exterior wall surface that contacts an interior surface of a vessel upon radial expansion of the stent.

In accordance with an aspect of the invention the membrane is attached to the frame by placing the frame on a mandrel; providing a solution of the polymer in an organic solvent such as toluene; dipping the frame and the mandrel into the solution; withdrawing the frame and the mandrel from the solution; thereafter drying the frame and the mandrel; and finally removing the mandrel from the frame. The steps of dipping and drying are preferably performed at room temperature.

BRIEF DESCRIPTION OF THE DRAWING

For a better understanding of these and other objects of the present invention, reference is made to the de-

tailed description of the invention which is to be read in conjunction with the following drawings, wherein:

FIG. 1 is a side elevation of an unexpanded stent in accordance with the invention supported on a mandrel;

FIG. 2 is a view similar to FIG. 1 showing the stent mounted about a collapsed balloon catheter inserted in a blood vessel; and

FIG. 3 is a view similar to FIG. 3 on a reduced scale showing the expanded stent in position in a blood vessel for holding the blood vessel in an open configuration;

FIG. 4 is a sectional view through line 4—4 of FIG. 3;

FIG. 5 is a side elevation similar to FIG. 1 of an unexpanded stent in accordance with an alternate embodiment of the invention;

FIG. 6 is a sectional view of a diseased blood vessel illustrating the stent of FIG. 5 expanded therein; and

FIG. 7 is a sectional view through line 7—7 of FIG. 6.

DESCRIPTION OF THE PREFERRED EMBODIMENT

Turning now to the Drawing, there is shown in FIG. 1 a stent 10 in accordance with the present invention carried on a mandrel 12 during manufacture. As taught in the '483 Patent, a wire frame or sleeve 11 of the stent is formed by first taking a fine wire 14 having a diameter of approximately 0.004", preferably made from platinum, and forming it into a generally sinusoidal form, in which approximately ten cycles or segments per inch are formed in the wire. These bends can be formed in any convenient manner, for instance as by bending about a rack gear by running a corresponding spur gear over a wire laid along the rack. The next step is to take the wire 14 and to further bend it into a serpentine or figure eight configuration so that the edges of each loop touch and abut the adjacent edges of the next loop forming the tight-looped serpentine ribbon form 16. In this configuration, approximately forty loops per inch of ribbon are present and the height or "amplitude" of the loops is approximately 1/16". This is accomplished by mechanically bending the partially formed loops 18, 18 up against each other into the tear-drop shapes shown in FIG. 1. The fine wire 14 used to form the basic flat ribbon 16 is a soft platinum wire that has been fully annealed to remove as much spring memory as possible. The straight wire before bending, being in the fully annealed condition, retains whatever shape it is formed into. After the flat narrow serpentine ribbon 16 is formed, it is wrapped about a mandrel 12 having a diameter of 0.060" in a spiral or helix fashion with the edges of each helix wrap of the ribbon 16 basically touching the adjacent ribbon helix edges to form the wire sleeve 11. The number of convolutions of the helix on the mandrel determines the length of the sleeve 11, and a typical stent of this type may have a length of approximately one and one-half inches. As the serpentine ribbon 16 of FIG. 2 is wound on the mandrel 12, the pigtail 20 of the wire 14 is inserted through the helix, as may be seen in FIG. 1. In actual practice, the ribbon 16 is wound about the mandrel 12 over top of the pigtail 20 of the wire 14. After the helix is formed to the desired length, the free end of the pigtail 20 extending through the helix is trimmed and welded smoothly to the final turn of the helix so as not to present any increased profile, and so as not to puncture or pierce the balloon catheter or the blood vessel into which it is being inserted. The end turn of the helix is welded at 22 and intermediate welds such as 24 are formed to stabilize the length of the helix. The first turn of the helix at the other end may also be welded to the pigtail at 26 so that the overall length of the stent can be constrained and maintained in the desired configuration.

After formation of the wire sleeve 11, a synthetic polymer membrane 28 is bonded to the sleeve 11 to form an impermeable wall or barrier. The membrane 28 should be a hypoallergenic, biologically inert material, that is free of latex rubber proteins and processing chemicals that can cause adverse reactions. The material is preferably Tactylon®, available from Tactyl Technologies, Inc., of Vista, Calif. Tactylon is well known to have properties of elasticity, distensibility and barrier protection without the sensitization problems associated with natural rubber.

The attachment of the polymer membrane 28 to the sleeve 11 is accomplished by dipping the sleeve 11 and the mandrel 12 into a solution of Tactylon in an organic solvent such as toluene at room temperature. The solution permeates the wire sleeve 11, coating the wires thereof. The sleeve 11 and mandrel 12 are then withdrawn from the solution and allowed to dry at room temperature. During drying the polymer forms a membrane 28 that spans the interstices of the sleeve 11, and the result is a continuous impermeable membranous wall that incorporates the wire sleeve 11 and covers the gaps and interstices in the sleeve's ribbon and helical substructures. The presence of the mandrel 12 during the development of the membranous wall assures that the lumen of the sleeve 11 remains patent, and that the ends of the sleeve 11 remain open. When the mandrel 12 is removed, the final stent 10 is an impermeable wire-reinforced tube or cylinder which is open at each end.

The stent 10 is used by placing it about the inflatable distal portion of a conventional collapsed balloon catheter 30 as shown in FIG. 2. In this configuration, the sleeve 11 generally has a diameter in the neighborhood of 1.5 mm for insertion into the coronary arteries. In a known manner the balloon catheter 30 with the stent 10 mounted thereon is inserted into the appropriate blood vessel 40. The stent 10 is guided to the desired location where there is an occluding plaque 38 or an aneurysm or other imperfection requiring placement of a stent. As the stent is passed through a stenotic segment of the vessel 40, the membrane 28 presents a smooth surface that gently glides along the intima 42 of the vessel 40, and is unlikely to abrade the endothelium, or create small intimal tears, or otherwise traumatize the plaque 38 so as to produce intramural hemorrhage. Once the stent 10 is properly located and verified by fluoroscopic or other technique, the balloon catheter 30 is inflated to radially expand the serpentine wire sleeve 11. As the balloon expands, it expands the tight tear drop bends of the serpentine ribbon 16 as explained in detail in the '483 Patent. For instance, in a particular embodiment where the diameter of the stent on the collapsed balloon catheter was 1.5 mm, the stent 10 has been expanded to 4–5 mm within the blood vessel 40 as shown in FIG. 3. The expanded stent maintains good interior surface support of the blood vessel by maintaining the close spacing of the wire loops and helices forming the sleeve. The reinforced impermeable membranous wall 28 is believed to attenuate the pulsatile hydraulic forces that are experienced by the segment of the blood vessel 40 in contact therewith and thereby prevent the enlargement or rupture of an aneurysm. The stent 10 is thus particularly

suitable for the mechanical stabilization of vascular aneurysms.

The expanded condition of the stent is shown in FIGS. 3 and 4 with the balloon catheter 30 having been removed. The stenotic segment is now dilated and the lumen of the vessel 40 is enlarged. In a case where the abnormal segment of the vessel 40 has an aneurysm, it is believed that the impermeable membrane 28 as reinforced by the wire sleeve 11 can prevent the dislodgement and subsequent embolization of fragments of plaque and thrombus that sometimes form in aneurysms. Also since the wire pigtail has no sharp ends and the free end is welded to the loop of the helix, there are no sharp edges or points to tear or catch on the catheter balloon or the interior surface of the blood vessel. Thus the stent of the present invention can be readily manipulated to the desired location. In prior art devices where the necessary surface support had to be achieved by heavier wire or a denser sleeve, it became difficult to flex the sleeve so as to transit the convoluted blood vessels. When a looser wire configuration was employed, the stability of the stent was decreased and the ultimate efficacy of the implanted stent compromised.

Turning now to FIGS. 5 and 6, there is shown an alternate embodiment of a stent 110 in accordance with the invention. In FIG. 5 an unexpanded stent 110 is similar to the first embodiment, except now the membrane 128 only forms a wall of a central portion 131 of a wire sleeve 111, and does not extend to end portions 133, 133'. In FIG. 6 there is shown the stent 110 which has been conventionally implanted in a diseased blood vessel 140, and has been in place for a sufficient period for tissue reaction to occur. The diseased portion of the vessel 140 is shown as an enlarged segment 141, the diseased condition typically being an aneurysm with a mural thrombus, or a plaque that has now been dilated by the radially expanded stent 110. The impermeable membrane 128, reinforced by the wire sleeve 111, is in sealing and stabilizing contact with the intimal surface of the diseased segment 141, and the lumen 143 of the stent 110 is patent, allowing free flow of blood therethrough. In the end portions 133, 133' there are open interstices of the wire sleeve 111, so that contact between the stent 110 and the intimal surface of the vessel 140 is limited to the wire 114. This allows a tissue reaction (shown as dark areas 137, 137) to develop about the end portions 133, 133', and firmly incorporate the end portions 133, 133' of the stent 110 into the wall of the blood vessel 140.

The stent 110 is manufactured in much the same way as that of the first embodiment. It is necessary, however to shield the end portions 133, 133' from contact with the non-latex polymer solution. This can be accomplished mechanically by a folded protective sheath or similar. The sheath is removed with the mandrel after drying.

It will be understood that the benefits of the impermeable membrane are not limited to the particular frame embodiments disclosed herein. The membrane can be applied to other frame constructions that are known to the art.

While this invention has been explained with reference to the structure disclosed herein, it is not confined to the details set forth and this application is intended to cover any modifications and changes as may come within the scope of the following claims:

What is claimed is:

1. A radially expandable stent for intravascular implantation comprising:

a tubular structure having a longitudinal axis, a radius, a central portion, and first and second ends, said tubular structure comprising a distensible frame and an impermeable distensible membrane interconnecting portions of said frame to form an impermeable wall surface disposed between said first and second ends about said axis, said tubular structure being adapted to receive an inflatable catheter for intra vascular placement and radial expansion therewith, wherein said membrane is disposed on said central portion and at least one of said first end and said second end is not in contact with said membrane;

whereby expansion of said catheter and said tubular structure brings said wall surface into supporting contact with an interior surface of a vessel.

2. The stent in accordance with claim 1, wherein said membrane comprises a synthetic non-latex, non-vinyl polymer.

3. The stent in accordance with claim 1, wherein said frame comprises a fine wire.

4. The stent in accordance with claim 1, wherein said membrane extends from said first end to said second end.

5. The stent in accordance with claim 1, wherein neither said first end nor said second end is in contact with said membrane.

* * * * *

United States Patent [19]

Sasaki et al.

[11] **Patent Number: 5,035,249**

[45] **Date of Patent: Jul. 30, 1991**

[54] **METHOD OF MAKING ENVELOPE FOR TISSUE EXPANDER**

[75] Inventors: **Gordon H. Sasaki**, Pasadena, Calif.; **Eugene R. Jakubczak**; **John R. D. Gauger**, both of Cordova, Tenn.

[73] Assignee: **Dow Corning Wright Corporation**, Arlington, Tenn.

[21] Appl. No.: **426,137**

[22] Filed: **Oct. 20, 1989**

Related U.S. Application Data

[62] Division of Ser. No. 356,313, May 24, 1989, Pat. No. 4,899,764, which is a division of Ser. No. 134,331, Dec. 17, 1989, Pat. No. 4,841,992.

[51] **Int. Cl.**[5] **A61F 2/12**

[52] **U.S. Cl.** **128/899**; 623/8; 623/901

[58] **Field of Search** 623/7, 8, 901, 11, 12; 128/899

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Primary Examiner—Randall L. Green

Assistant Examiner—David H. Willse

Attorney, Agent, or Firm—John L. Chiatalas

[57] **ABSTRACT**

A tissue expander and a method of making a tissue expander which includes (a) a fluid-tight envelope which is inflatable by a single means for inflation and which has an expandable upper section formed of (i) a first elastic portion and (ii) a second elastic portion formed of a material having a lower modulus of elasticity than that of the material forming the first portion, so that during the inflation of said envelope the modulus of elasticity of each portion at least partially controls the amount of expansion of each portion, thereby allowing the envelope to assume a complex shape. The tissue expander also has a means for inflating the envelope with a biocompatible fluid.

13 Claims, 3 Drawing Sheets

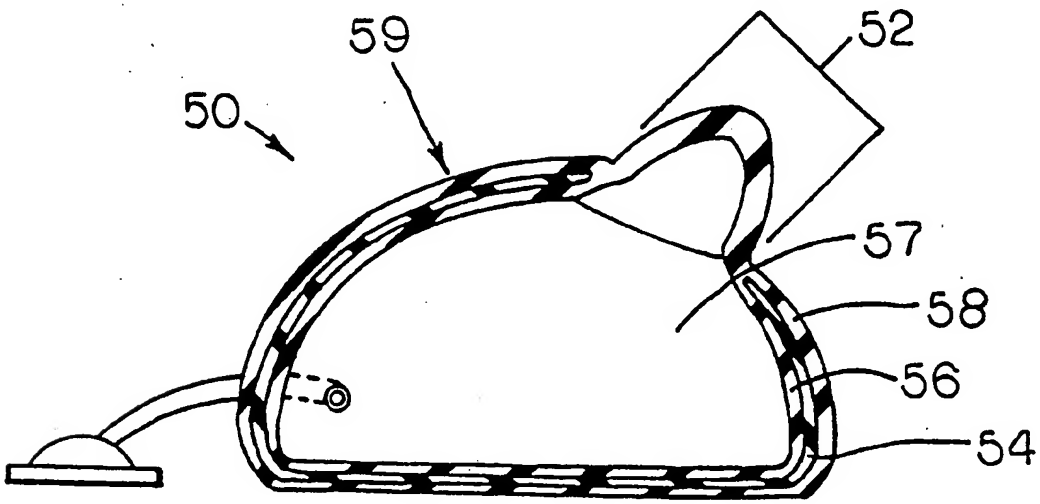


Fig. 1

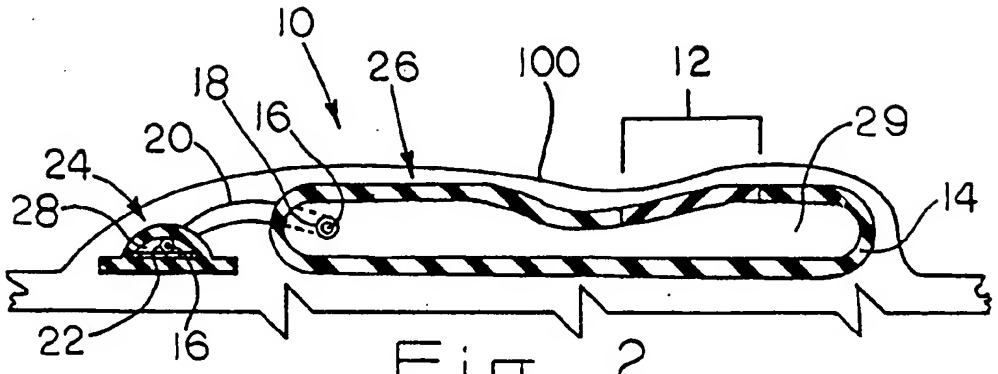


Fig. 2

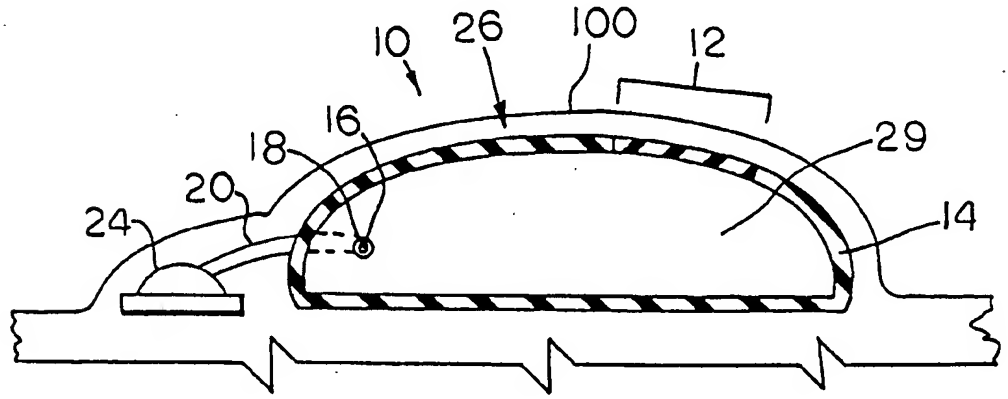


Fig. 3

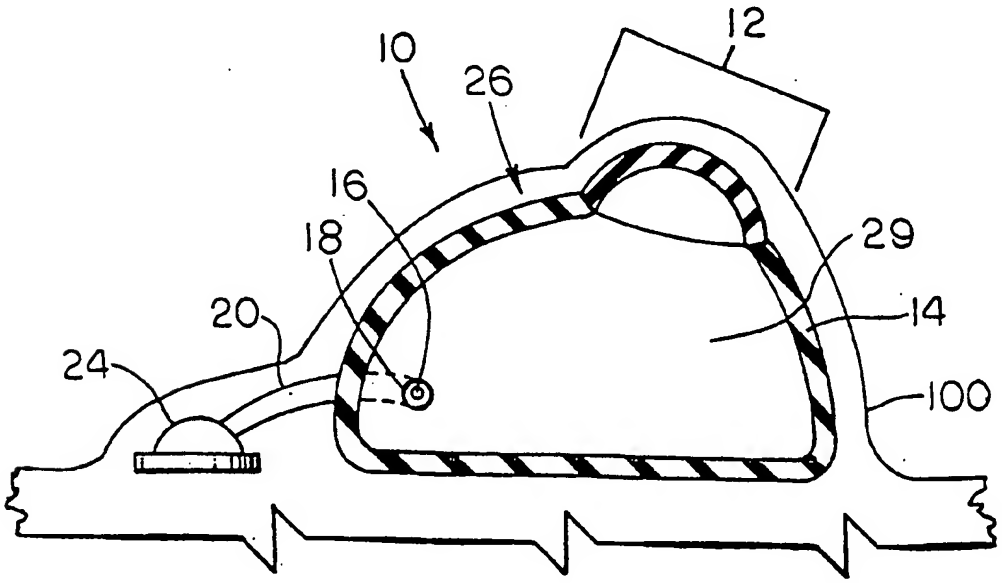


Fig. 4

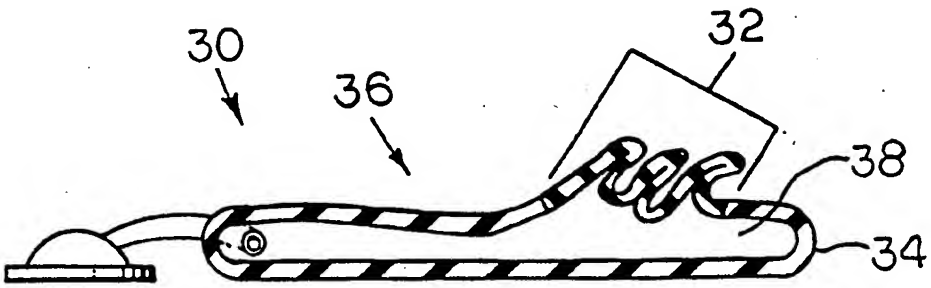


Fig. 5

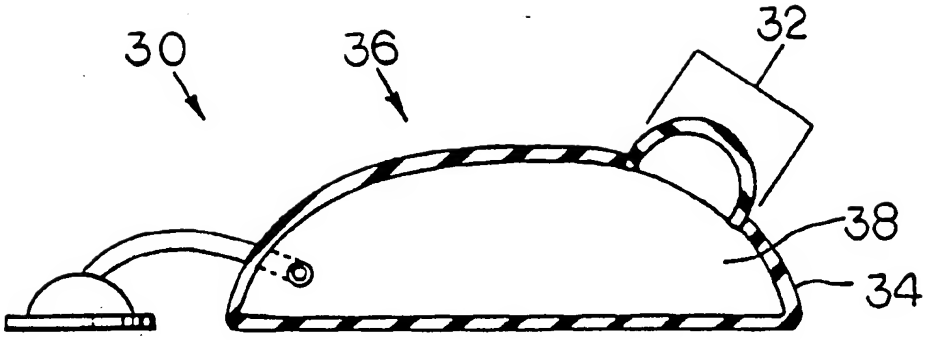


Fig. 6

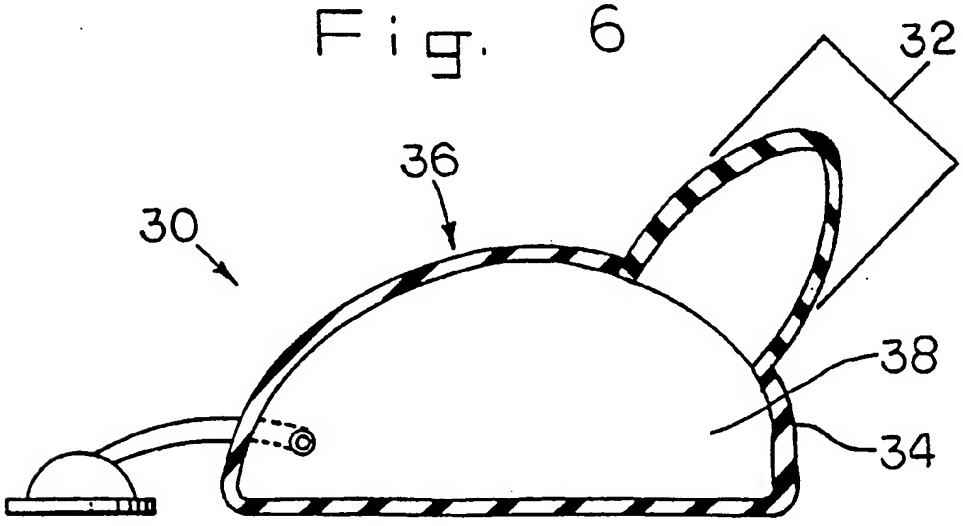


Fig. 7

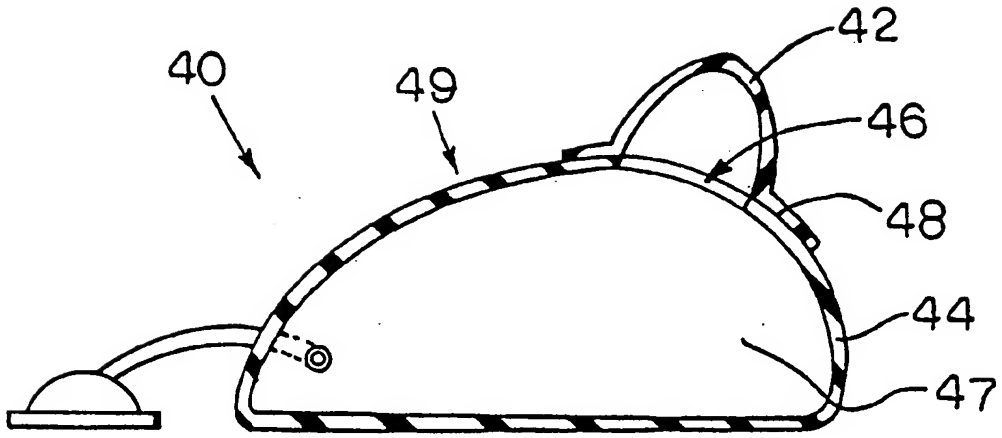
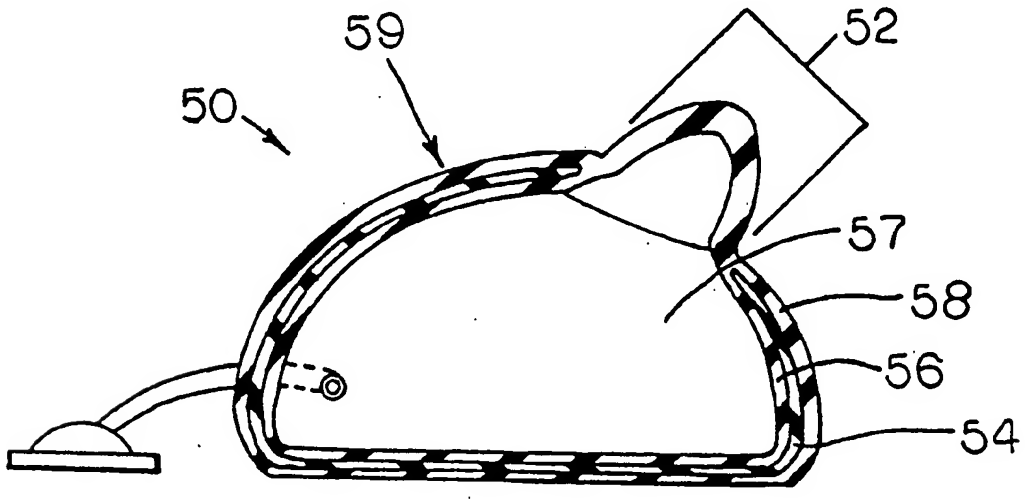


Fig. 8



METHOD OF MAKING ENVELOPE FOR TISSUE EXPANDER

This is a divisional of co-pending application Ser. No. 07/356,313 filed on 5/24/89, now U.S. Pat. No. 4,899,764, which is a divisional of application Ser. No. 07/134,331 filed on 12/17/89, now U.S. Pat. No. 4,841,992.

BACKGROUND OF THE INVENTION

The present invention relates to tissue expanders, including tissue-expanding mammary prostheses and to methods of making and using such tissue expanders. More particularly, the invention relates to tissue expanders capable of expanding overlying tissue into a complex shape.

Subcutaneous tissue expanders have come into wide use because of the variety of plastic surgical procedures that have been developed which either require that tissue be expanded to receive or retain an implant or that a flap of tissue be generated for use on some other part of the body.

Of the tissue expanders known in the art, some provide for expanding tissue differentially, that is, into a preselected complex shape. For example, U.S. Pat. No. 4,574,780 to Manders discloses tissue expanders which are capable of differentially expanding skin. Manders disclose that the differential expansion can be accomplished by using a tissue expander having a limited expansion portion and a differential expansion portion. The patent teaches that one way of creating a limited expansion portion is by making the expander wall of that portion thicker than the differential expansion portion. Manders also discloses that the limited expansion portion may be created by reinforcing the portion. A commercial example of a tissue expander which uses the Manders invention is SILASTIC ® Differential Tissue Expander. H.P. sold by Dow Corning Wright. Arlington, Tenn.

U.S. Pat. No. 4,651,717 to Jakubczak discloses another type tissue expander which is capable of expanding tissue into complex forms. This tissue expander consists essentially of at least two separately inflatable envelopes wherein one is used as a base and the other is smaller in volume than the first and is attached to the upper half of the base envelope to expand the tissue overlying the second envelope to a greater extend than is accomplished by the first envelope. This device requires that each envelope has an inflation means associated therewith that is separate from the other envelope's inflation means.

European Patent 196,821 discloses a tissue expander system wherein Dacron mesh may be embedded in members of the tissue expander to provide directional expansion of the tissue expander.

An implantable mammary prosthesis which can be partially inflated after the prosthesis is inserted beneath the skin is shown in product data sheet number 120318 dated 10/77 from the McGhan Medical Corporation of Santa Barbara. Calif. entitled "Reconstructive Mammary Implant (Birnbaum Design)" which shows a dual envelope mammary prosthesis where one part of the prosthesis has a gel-filled envelope and the other integral envelope along side the first is inflated with saline after implantation. Use of this prosthesis is described in a November, 1976, article entitled "Customized Reconstruction of the Breast After Radical and Modified

Radical Mastectomies" by Birnbaum. et al. in *The Western Journal of Medicine* on pages 388-390. U.S. Pat. No. 4,643,733 to Becker discloses another implant which is a subcutaneous expander and a permanent reconstruction implant.

In the catheter art. U.S. Pat. No. 4,222,384 to Birtwell discloses a catheter formed from silicone rubber wherein the tip and balloon portion are molded in a single integral piece in a suitable mold but in a manner in which the tip portion of the mold is loaded with a parison of silicone rubber which will be stiff when cured and with the balloon portion of the mold being loaded with a parison of compatible silicone rubber which will be more elastic when cured.

In addition, U.S. Pat. No. 3,831,583 to Edmunds. Jr.. et al. discloses an implantable device for restricting the flow of blood through a major blood vessel which includes (1) a ring, capable of inward distention. (2) a non-distensible bulb, and (3) a non-distensible tube. The patent also mentions that silicone rubber of varying degrees of hardness or cure can accommodate the need for the distensible or non-distensible portions.

SUMMARY OF THE INVENTION

In view of the tissue expander devices discussed above,there remains a need for a tissue expander which can shape overlying tissue into a complex shape and (1) can be made with existing manufacturing equipment. (2) whose characteristics can be easily altered to suit many applications. (3) is formed of biocompatible materials. (4) is relatively easy and quick to make and uses a minimum of parts. (5) can have a minimum number of injection sites therefore having a minimum number of injection button connections and minimizing the number of times a patient needs to be injected, (6) can have a uniform wall thickness, (7) is relatively economical, (8) has relatively low rejection rates during production, and (9) provides the surgeon with good control of differential expansion.

These and other objects can be provided by the implantable tissue expander of the invention which comprises (a) a fluid-tight envelope which is inflatable by a single means for inflation and which has an expandable upper section comprising a first elastic portion and a second elastic portion formed of a material having a lower modulus of elasticity than the material forming the first portion,so that during the inflation of the envelope the modulus of elasticity of each portion at least partially controls the amount of expansion of each portion and causes the envelope to assume a complex shape and (b) means for inflating the envelope with a biocompatible fluid associated therewith for the controlled inflation of the envelope. The tissue expanders of the invention are also suitable for inflatable-type mammary prostheses. The invention also provides a method of making an envelope for such a tissue expander and a method of using such a tissue expander.

BRIEF DESCRIPTION OF THE DRAWINGS

The above and other objects and advantages of the present invention will become apparent to those skilled in the art upon an examination of the following description and drawings which are illustrative of the present invention.

In the Drawings:

FIG. 1 is a partial cross-sectional side view of one embodiment of the present invention shown as a substantially deflated tissue expander.

FIG. 2 is a partial cross-sectional side view showing the tissue expander of FIG. 1 after partial inflation.

FIG. 3 is a partial cross-sectional side view showing the tissue expander of FIG. 2 after further inflation.

FIG. 4 is a partial cross-sectional side view illustrating a second embodiment of the present invention shown as a substantially deflated tissue expander.

FIG. 5 is a partial cross-sectional side view showing the tissue expander of FIG. 4 after partial inflation.

FIG. 6 is a partial cross-sectional side view showing the tissue expander of FIG. 5 after further inflation.

FIG. 7 is a partial cross-sectional side view illustrating a third embodiment of the present invention shown as an inflated tissue expander.

FIG. 8 is a partial cross-sectional side view illustrating a fourth embodiment of the present invention shown as an inflated tissue expander.

DETAILED DESCRIPTION OF THE INVENTION

Referring to the Drawings, wherein like reference characters designate corresponding parts throughout the Figures thereof, FIG. 1 depicts one form of a tissue expander according to the invention shown as tissue expander 10 implanted beneath the skin 100 of a patient. Tissue expander 10 consists of a fluid-tight envelope 26 and means for inflating the envelope 26. The inflation means is shown in the form of injection button 24 of conventional design which is designed to permit inflation by addition of a biocompatible fluid such as isotonic saline into pocket 29 of envelope 26. As with such conventional injection buttons, a hypodermic syringe needle is used to introduce biocompatible fluid into the hollow region 28 of injection button 24. The fluid travels through the lumen of tube 20 from region 28 into pocket 29 of envelope 26 because the ends of tube 20 are sealed to injection button 24 and envelope 26 at attachment points 22 and 18 respectively, with, for example, a medical grade silicone adhesive such that the lumen 16 is in communication with region 28 and pocket 29.

Envelope 26 is formed from a bottom and an expandable upper section which together define pocket 29 which is inflatable by a single means for inflation. Means for inflation is shown as injection button 24. The expandable upper section has portions 12 and 14,both made of elastic material with portion 12 being formed of a material having a lower modulus of elasticity than the material from which portion 14 is formed. Although it is illustrated that the bottom of envelope 26 is formed of the same material as portion 14, this is not required for the invention. The bottom may be made of the same or different material than any other part of the expander.

FIG. 2 illustrates tissue expander 10 after some inflation. FIGS. 2–3 and 5–8 show the pockets inflated, but no inflation fluid is shown, for purposes of clarity. The fluid used to inflate the envelopes is preferably an isotonic saline solution although other biocompatible fluids which will remain under pressure within the envelope, such as a silicone gel, can also be used. In FIG. 2, portion 12 has not begun to expand at a faster rate than portion 14, and therefore envelope 26 has a generally smooth hemispherical shape. Resulting from the expansion of the envelope 26, skin 100 also has expanded and taken on the same general shape of envelope 26. The appearance of the tissue expanders of this invention will vary depending on the design and the materials used, therefore, the generally smooth shape is not necessarily achieved with every tissue expander of the invention but is shown here as a possible occurrence and for illustrational purposes.

FIG. 3 illustrates expander 10 which has been inflated to a greater degree than that shown in FIG. 2, wherein portion 12 has expanded more than portion 14 and therefore has caused envelope 26 and skin 100 to each assume a complex shape. This illustrates that the modulus of elasticity of each portion controls the amount of expansion of each portion. Stated another way, the different moduli of elasticity of the portions causes one portion to expand to a greater extent than the other portion some time during the expansion process. It is not necessary that the portion having the lower modulus expand to a greater extent throughout the entire inflation process, but at least during some period of the process. As can be seen with FIGS. 1–8, the envelope does not need to have varying wall thickness to achieve differential expansion.

In this example portion 12 stretches at a faster rate than portion 14. It is not necessary that portion 12 stretch at a faster rate than portion 14 throughout the entire inflation process, but when portion 12 stretches at a faster rate during at least part of the inflation process the envelope is expanded more at portion 12 than at portion 14 to achieve the differential expansion. Also, it is not necessary that one portion expands at a "faster rate" than another; two portions can expand at the same rate and achieve differential expansion. For example, an envelope formed of one material which when filled, but not yet expanded or stretched, has a first end which measures 1" high and a second end which measures 2" high. It is feasible that this envelope when stretched will take on a generally spherical shape so that each end has generally the same height. In contrast, when using the invention and making a similar envelope but where the first end is made from a material having a higher modulus of elasticity than the second end, expansion could result so that after some inflation the 1" high end expands to a height of 1½" and the 2" end expands to a height of 3". In this example, the moduli of elasticity of the materials controls the amount of expansion even though the two ends have expanded at the same rate over period of time: a 50% increase in height for each end.

FIGS. 4–6 illustrate another type of tissue expander according to the invention. FIG. 4 shows tissue expander 30 having envelope 36. Envelope 36 is formed of a bottom and an upper section, and the upper section is formed of portions 32 and 34, wherein portion 32 is formed of a material having a lower modulus of elasticity than the material which forms portion 34. In this embodiment, envelope 36 is pre-formed so that portion 32 has excess material and has folds when the envelope is in its deflated state.

FIG. 5 shows expander 30 after inflation of envelope 36. As can be seen in this illustration, portion 32 has already caused envelope 36 to take on a complex shape because the excess material has been filled with fluid. In FIG. 6, envelope 36 has been inflated beyond that shown in FIG. 5, showing that portion 32 has expanded relatively more than portion 34 and has caused envelope 36 to take on a different shape than that shown in FIG. 5.

FIG. 7 illustrates another embodiment of the invention shown as tissue expander 40 having envelope 49. Envelope 49 is shown in the inflated state. In this embodiment, portion 42 has a lower modulus of elasticity than portion 44. The peripheral area of portion 42 is

adhered onto a corresponding area of portion 44 surrounding an opening portion 46 in portion 42 which provides fluid communication between the spaces covered by portions 42 and 44. Portion 42 may be adhered by bonding to portion 44 or it may be adhered by using an adhesive between portions 42 and 44 at area of contact 48. As an example, a medical grade silicone adhesive can be used to adhere the two portions if silicone elastomers are used for the envelope. Alternatively, portion 42 could be laminated to the inside surface of portion 44, so long as it is placed below an opening in portion 44.

FIG. 8 illustrates a preferred embodiment of the invention shown as tissue expander 50 with envelope 59. Envelope 59, shown in the inflated state, has an inside elastic layer 56 which extends around the entire envelope, an intermediate elastic layer 54 which extends only partially around the envelope, and an outside layer 58 which extends around the entire envelope. Inside layer 56 and outside layer 58 are formed of the same material, whereas intermediate layer 54 is formed of a material having a higher modulus of elasticity than the other two layers. The area of envelope 59 which is deficient of the material which forms layer 54 expands further than the remainder of envelope 59, because the composite of the remainder of the envelope includes a material which has a higher modulus of elasticity than the area of envelope 59 which is deficient of layer 54.

Envelope 59 is prepared by first coating a mandrel with a layer of a first polymeric composition, then coating almost all of the coated mandrel with a second polymeric composition which has a higher modulus of elasticity than the first composition leaving a space on the coated mandrel uncoated with the second composition, and then coating the mandrel with the first composition again so that the space left uncoated with the second composition is covered with the first composition. The composite compositions are then cured and removed from the mandrel. It is preferred that silicone elastomer compositions are used for the first and second compositions and, if they are used, generally the compositions will bond together upon curing. However, the two compositions do not necessarily have to be capable of bonding together.

Variations on this technique are possible. For example, one could eliminate the inside layer 56 or the outside layer 58 altogether and achieve similar results. One could also use three or more polymeric compositions each with different moduli of elasticity, so long as at least one area of the envelope has a lower modulus of elasticity than the envelope wall surrounding that area, so that a complex shape may be achieved.

Although the figures illustrate the combination of only two portions to form the expandable upper section, one being formed of a material having a lower modulus of elasticity than the other, devices of the invention may include more than two portions, where the materials forming the portions could each have a different modulus of elasticity.

The invention is also suitable for making inflatable mammary prostheses which are implanted, used to differentially expand tissue, then left in the body as prostheses. For example, such a mammary prosthesis could be similar to any of the expanders shown in the FIGS. 1-8. Another proposed design would be to have a double lumen mammary prosthesis having a chamber inside another chamber, where one chamber is optionally pre-filled with a gel. The unfilled chamber would be composed of at least two materials having different moduli of elasticity to provide for the differential expansion. Preferably, the unfilled chamber is the interior chamber and the gel-filled chamber is the exterior chamber. Having the gel-filled chamber on the outside would help protect the interior chamber and, in case of a rupture, help minimize leaking of the fluid used to fill the interior chamber A tissue expander or a mammary prostheses using this invention may also have side-by-side or stacked chambers where one is pre-filled or neither is pre-filled.

The tissue expander of the invention may have a remote injection button as shown in the figures or may have an injection button mounted directly on the envelope. One example of an injection button which can be used with this invention is found in U.S. Pat. No. 4,190,040 to Schulte. Another injection button which can be used on the envelope is of the type described in U.S. Pat. No. 4,428,364 to Bartolo. As an alternative to using percutaneous means for inflating the tissue expander, one could use the teachings of Austad in U.S. Pat. No. 4,157,085 which teaches osmotically expandable tissue expanders. The bottom of the envelopes may be substantially non-extensible, e.g.. using the teaching of Radovan in U.S. Pat. No. 4,217,889.

Although it is illustrated in the figures that the portion formed of the material with the lower modulus of elasticity is smaller than the other portion, envelopes according to this invention may be formed where the larger portion is formed of the material with the lower modulus of elasticity.

The envelopes of this invention can also be formed with varying wall thicknesses or embedded materials for limiting expansion so that the expansion of the envelope is controlled by both the moduli of elasticity of the materials of construction and another means. There are several advantages of making the envelopes according to this invention whether or not in combination with other ways of controlling expansion. Envelopes of this invention have the potential of being relatively thinner than envelopes solely using varying wall thicknesses to control expansion and still achieve the desired amount of differential expansion. Therefore envelopes of this invention can use less material and reduce the cost of making, can be faster and easier to make because thinner walls require less application of the polymeric composition to a mandrel, if a mandrel is used and can cure faster than the thicker envelopes. In addition, when less material and/or fewer applications of the material are required to make the envelopes there is less chance for dirt pick-up and bubble formation between applied layers and therefore improved overall quality of the envelope results.

The envelopes of this invention are preferably constructed of biocompatible silicone elastomers similar to the medical grade silicone elastomers commonly used in the manufacture of mammary implants or tissue expanders (e.g. those which are available from Dow Corning Corporation, Midland. MI 48686), but could be manufactured of other biocompatible elastic materials such as polyurethanes. It is preferred that silicone elastomers which cure via $\equiv SiH$ to $CH_2=CHSi\equiv$ addition, in the presence of a catalyst, such as a platinum catalyst, are used. When using silicone elastomers as the materials for forming portions 12 and 14, the level of the filler, preferably, fumed silica to control the modulus of elasticity has been found to work well. The envelopes can be formed in various ways, e.g. by applying a suitable

solution to a mandrel as discussed or, in the case of silicone envelopes, by adhering two sheets of vulcanized elastomer together by imposing an unvulcanized washer between the sheets at the perimeter and curing the washer to the elastomer sheets while applying pressure to the perimeter.

As discussed previously, portion **12** is formed of a material having a lower modulus of elasticity than the material used to form portion **14**. Modulus of elasticity can be defined as the applied force per unit of original cross sectional area of a test bar of the material at a specific percentage elongation (or tensile stress at a given elongation). Although any difference in tensile stress at a given elongation would suffice for the invention. We have found that a silicone elastomer for portion **12** having a tensile stress of about 200 psi at 100% elongation works well with a silicone elastomer for portion **14** having a tensile stress of about 500–700 psi at 100% elongation. The tensile stresses were measured by a procedure based on ASTM D 412. In this case, the modulus of elasticity of the more elastic material is as preferred, less than half of the modulus of elasticity of the less elastic material. Using materials wherein one has a modulus of elasticity of less than about 75% than the other would also be highly suitable.

As mentioned, a preferred way of making materials having a difference in moduli of elasticity is by changing the level of filler in the polymeric compositions. By adding more filler to a composition, the modulus of elasticity is increased, resulting in a stiffer material. For example, on page 217 of the book, *Principles of Polymer Systems* (1970), by Ferdinand Rodriguez, the effect of fillers on polymer characteristics is discussed along with the fact that the addition of carbon black in a crosslinked natural rubber shows an increase in stiffness with increase in filler loading.

Another way of forming materials with varying moduli of elasticity is by varying the crosslink density (or level of cure) or molecular weight with or without changes in filler level, wherein generally, compositions with higher crosslink density have higher moduli. The phenomenon of altering the modulus of elasticity with changes in crosslink density or level of cure is discussed on pages 77–89 of the book, *Vulcanization of Elastomers* (1964), edited by G. Alliger and I. J. Sjothun. Another way of acquiring two materials with different moduli is by using materials which have a different polymer base. e.g. where one portion is formed from silicone-polyurethane copolymers and the other is silicone. Another way is by the addition of plasticizers one can create a material with a lower modulus of elasticity. This phenomena is discussed on pages 45–46 of *Principles of Polymer Systems*.

To make the envelopes of the invention any known fabrication technique may be used. For example, the envelopes can be formed by coating a mandrel (by spraying, brushing, dipping, rolling, etc.) with an uncured polymeric composition and, subsequently, curing the composition, or they may be formed by adhering two sheets of elastic material together When the envelope is formed by using a mandrel with rounded edges, the envelope has the further advantage of not having any sharp, rigid, or elevated edges which may cut into the patient's tissue and cause discomfort and/or other complications. The portions of the upper section responsible for the differential expansion, may be adhered to the envelope by bonding or adhering two bodies of material together with a suitable adhesive.

Having described several embodiments of the tissue expander, the manner in which it can be used will now be described with reference to FIGS. **1–3**. It is to be understood that tissue **100** would rest directly upon expander **10** and button **24** when expander **10** is implanted. In FIG. **1**, a partial cross-sectional side view of substantially deflated tissue expander **10** is shown implanted beneath tissue **100** to be expanded according to surgical procedures familiar to those skilled in the art of implantation of tissue expanders. Tissue expander **10** is placed in a surgically-formed opening beneath tissue **100**. If means for attaching tissue expander **10** are present it would be used to attach the device to underlying body members and thus help hold envelope **26** in a preselected orientation with respect to the tissue to be expanded. Such means could be, for example, fixation tabs which can be strips of polyester fiber mesh reinforced silicone elastomer fixed to the lower portion of the envelope such as by means of a medical grade silicone adhesive. These tabs would then be sutured to underlying body members, e.g. muscle or fascia. A needle of a hypodermic syringe which contains a biocompatible fluid is then passed through tissue **100** and injection button **24** and then fluid is gradually forced into hollow region **28** and, in turn. travels through tube **20** and into interior region **29** of envelope **26**. Such injections are done periodically over an extended period of time. Envelope **26** is inflated with the biocompatible fluid in a well known manner at such a rate that the tissue **100** is expanded over a reasonably short period of time, but not so short a time that tissue necrosis occurs. FIG. **2** shows tissue expander **10** after some inflation and FIG. **3** shows tissue expander **10** after inflation beyond that shown in FIG. **2** and enough inflation to see differential expansion, resulting in the tissue taking on a complex shape.

After the envelope has been inflated to the desired degree, tissue expander **10** may be surgically removed and a prosthesis may be surgically implanted in its place or the expander may be left in as a prosthesis.

These and other variations of the present invention may be made which fall within the scope of the appended claims even though such variations were not specifically discussed above.

What is claimed is:

1. A method of making an envelope for a tissue expander having a single means for inflation, said method comprising the steps of:

(a) applying a first fluid elastomeric polymer composition, capable of forming a first cohesive elastic layer stretchable to at least about 50% of its unstretched length, to less than the entire surface of a mandrel, leaving at least one section of the mandrel surface free of said first composition and capable of forming another cohesive layer thereon;

(b) applying a second fluid elastomeric polymer composition, capable of forming a second elastic layer stretchable to at least about 50% of its unstretched length, to selected other sections of the mandrel surface free of said first composition, so that the mandrel surface is substantially entirely covered with said fluid compositions;

(c) applying a third fluid polymeric composition at least partially covering said second composition, said third composition being capable of forming a third cohesive elastic layer; and

(d) forming said first, second and third cohesive layers from said applied elastomeric compositions into

a seamless three-dimensional envelope, said first and third layers each having a modulus of elasticity greater than said second layer, such that one area of said envelope has a greater modulus of elasticity than a surrounding area, allowing the envelope to assume a complex shape.

2. A method of making an envelope for a tissue expander having a single means for inflation, said method comprising the steps of:

(a) applying a first fluid elastomeric polymer composition, capable of forming a first elastic layer stretchable to at least about 50% of its unstretched length, to less than the entire surface of a mandrel, leaving at least one section of the mandrel surface free of said first composition and capable of forming another cohesive layer thereon;

(b) applying a second fluid elastomeric polymer composition, capable of forming a second elastic layer stretchable to at least about 50% of its unstretched length, to selected other sections of the mandrel surface free of said first composition, so that the mandrel surface is substantially entirely covered with said fluid compositions; and

(c) forming said first and second cohesive layers from said applied compositions into a seamless three-dimensional envelope, said first layer having a greater modulus of elasticity than said second layer, such that one area of said envelope has a greater modulus of elasticity than a surrounding area, allowing the envelope to assume a complex shape.

3. The method of claim 1 wherein step (a) is performed before step (b).

4. The method of claim 1 wherein step (b) is performed before step (a).

5. The method of claim 1 wherein step (d) is performed after steps (a) and (b).

6. The method of claim 2 wherein step (a) is performed before step (b).

7. The method of claim 2 wherein step (b) is performed before step (a).

8. The method of claim 1 wherein said second composition is capable of curing to said first composition upon forming cohesive layers from said applied compositions.

9. The method of claim 2 wherein said second composition is capable of curing to said first composition upon forming cohesive layers from said applied compositions.

10. The method of claim 1 wherein said second fluid composition is applied to the entire surface of the mandrel.

11. The method of claim 2 wherein said second fluid composition is applied to the entire surface of the mandrel.

12. The method of claim 1 wherein said compositions comprise different or the same elastomers.

13. The method of claim 2 wherein said compositions comprise different or the same elastomers.

* * * * *

US005527337A

United States Patent [19]

Stack et al.

[11] Patent Number: 5,527,337

[45] Date of Patent: Jun. 18, 1996

[54] **BIOABSORBABLE STENT AND METHOD OF MAKING THE SAME**

[75] Inventors: **Richard S. Stack**, Chapel Hill; **Howard G. Clark**, Durham, both of N.C.; **William F. Walker**, Holcomb, N.Y.; **James H. McElhaney**, Durham, N.C.

[73] Assignee: **Duke University**, Durham, N.C.

[21] Appl. No.: **200,556**

[22] Filed: **Feb. 22, 1994**

Related U.S. Application Data

[63] Continuation of Ser. No. 701,154, May 17, 1991, abandoned, which is a continuation-in-part of Ser. No. 658,708, Feb. 21, 1991, abandoned, which is a continuation-in-part of Ser. No. 524,884, May 18, 1990, abandoned, which is a continuation-in-part of Ser. No. 66,345, Jun. 25, 1987, Pat. No. 5,059,211, said Ser. No. 701,154, is a continuation-in-part of Ser. No. 649,534, Feb. 1, 1991, Pat. No. 5,306,286, which is a continuation of Ser. No. 66,345.

[51] **Int. Cl.**[6] **A61M 29/00**

[52] **U.S. Cl.** **606/198**; 623/901

[58] **Field of Search** 606/108, 198, 606/191, 151, 153–156; 623/1, 12, 901

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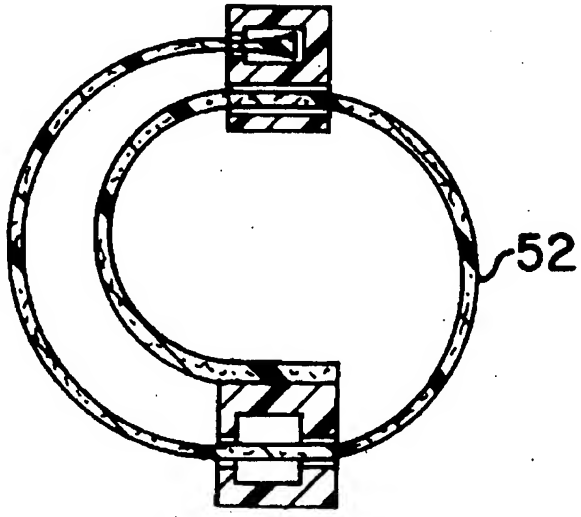
Primary Examiner—Michael H. Thaler
Attorney, Agent, or Firm—Cushman Darby & Cushman

[57] **ABSTRACT**

A bioabsorbable stent for placement at the locus of a stenotic portion of a body passage, such as a blood vessel, which is flexible and compliant for safe and effective delivery to the site of the stenotic portion of, for example, a blood vessel, and so as to avoid the disadvantages of chronic implantation, such as arterial rupture or aneurism formation while exposed to the continuous stresses of a beating heart. The stent is formed from a bioabsorbable material and is porous or has apertures defined there through to facilitate tissue ingrowth and encapsulation of the stent. The stent is encapsulated and biodegrades or bioabsorbs within a period of days, weeks or months as desired following encapsulation to thereby minimize the likelihood of embolization or other risks of the dissolved material and to avoid the disadvantages of chronic implantation.

14 Claims, 7 Drawing Sheets



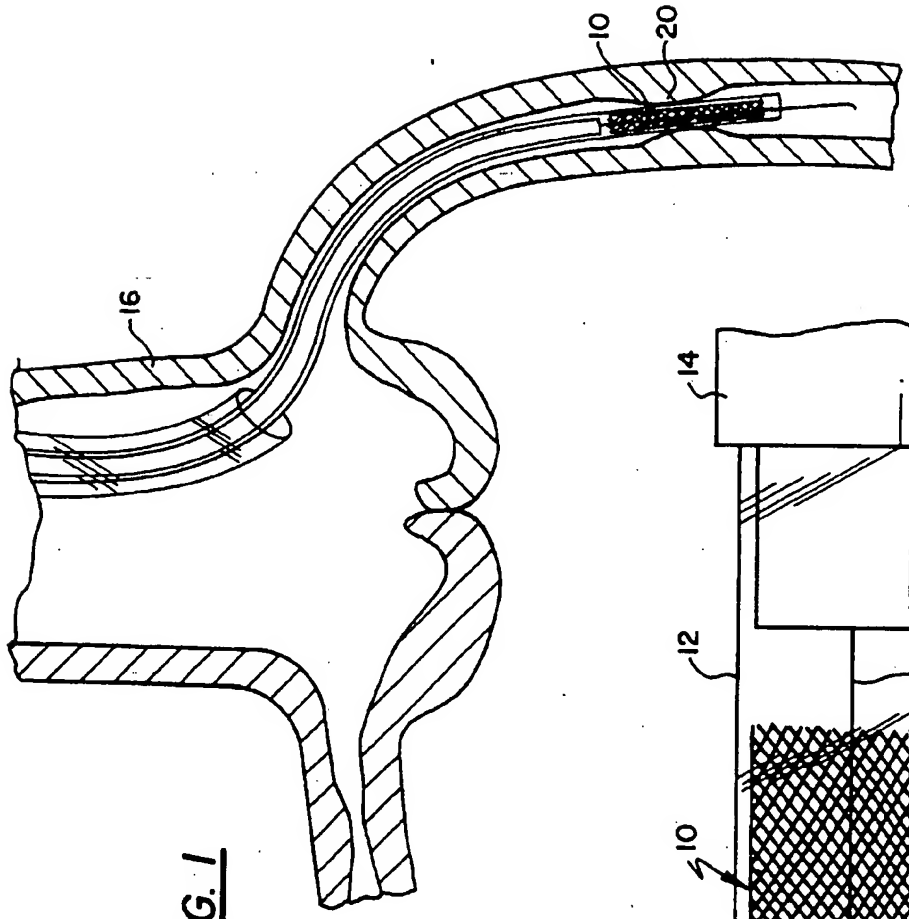


FIG. 1

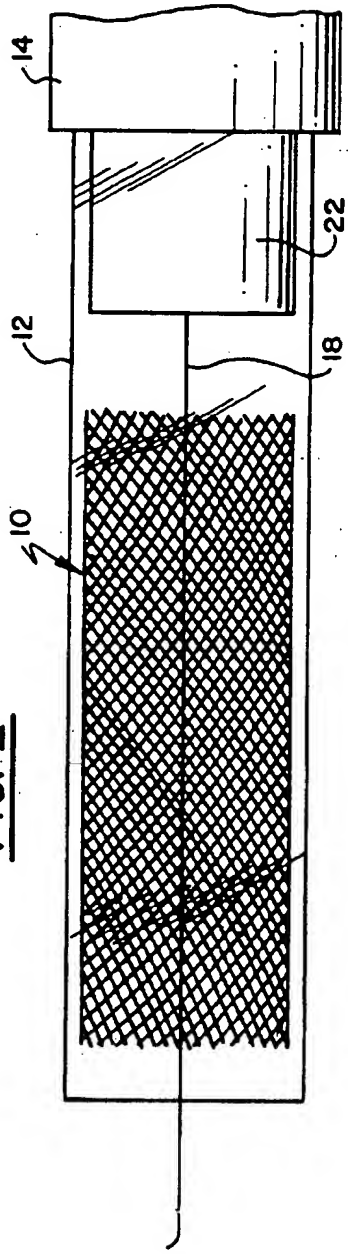


FIG. 2

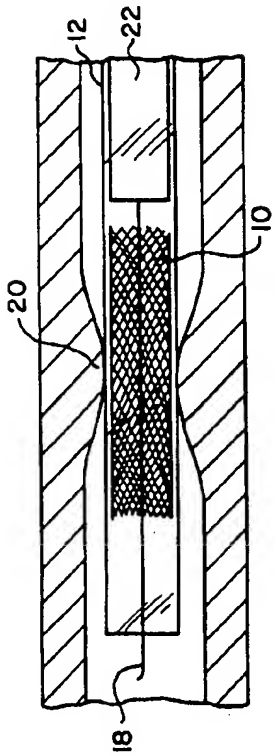


FIG. 3

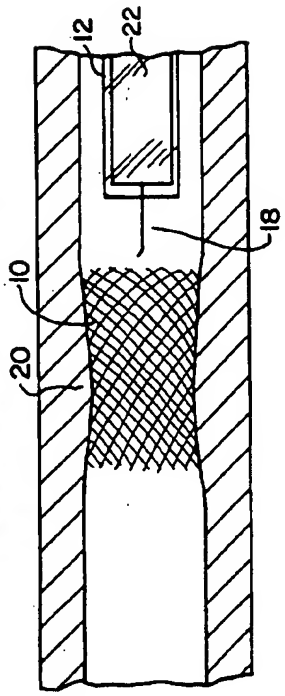


FIG. 4

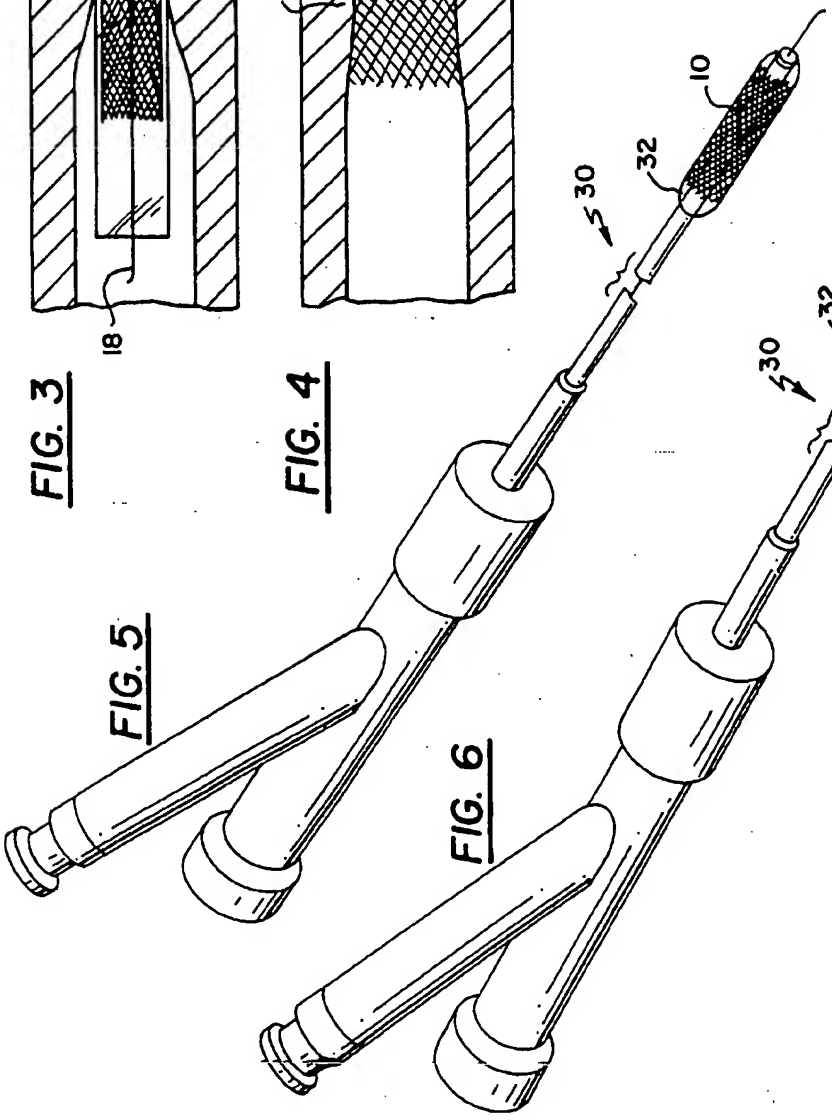


FIG. 5

FIG. 6

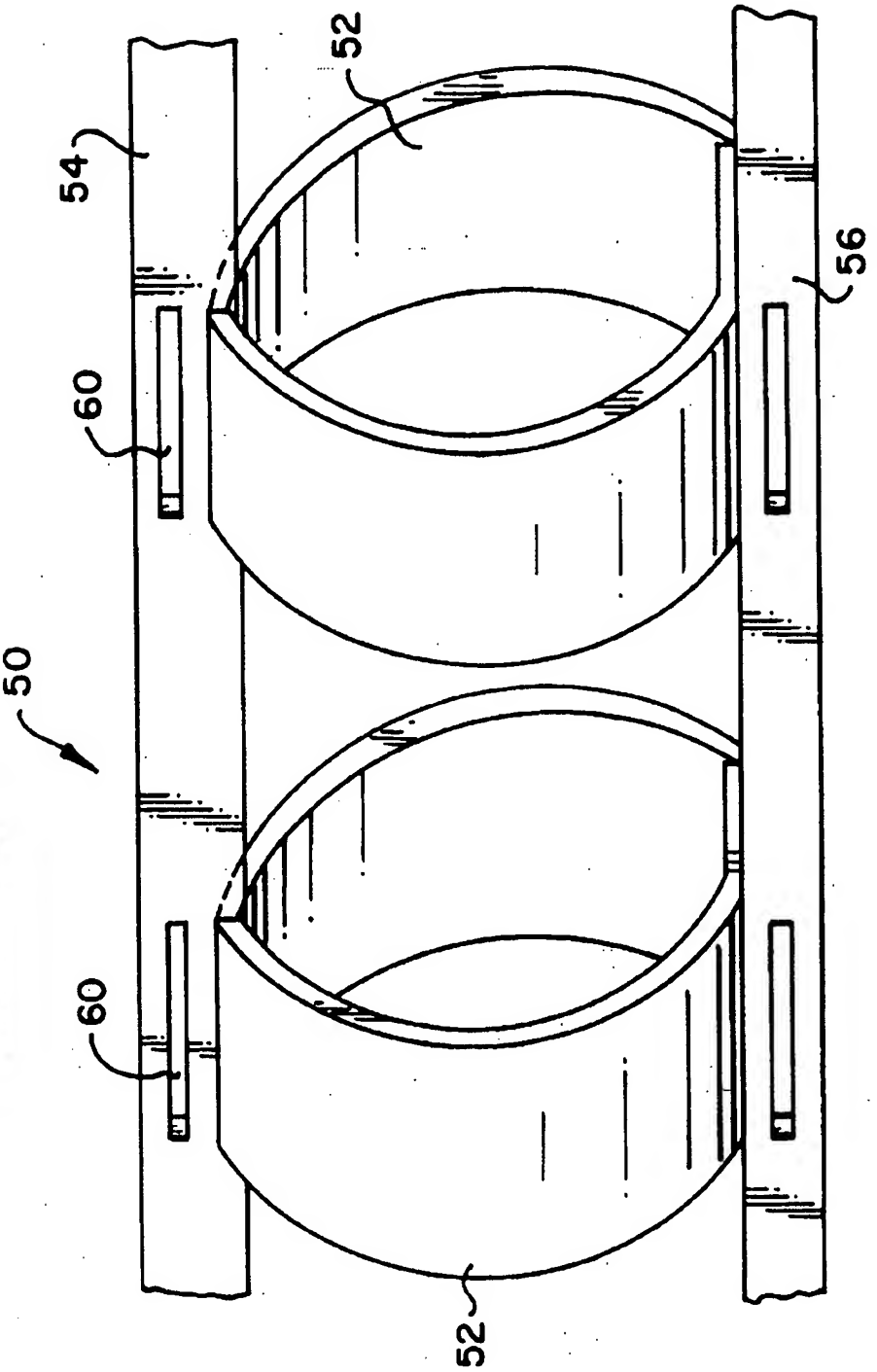


FIG. 7

FIG. 9

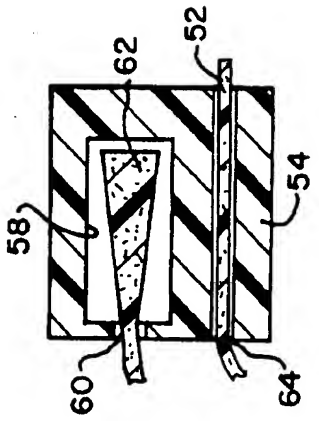


FIG. 10

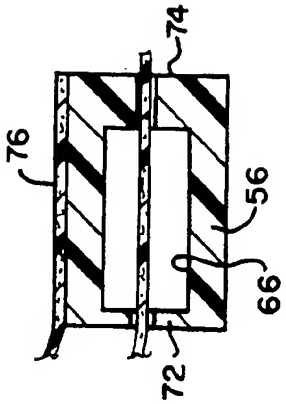
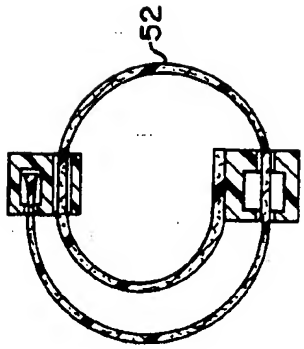


FIG. 8



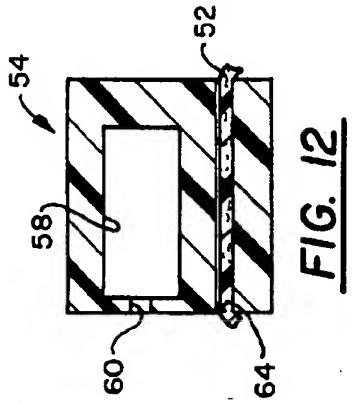


FIG. 12

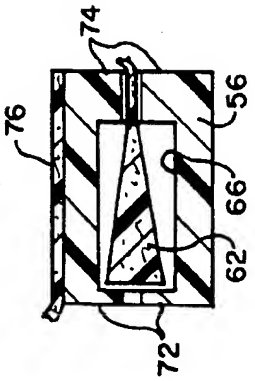


FIG. 13

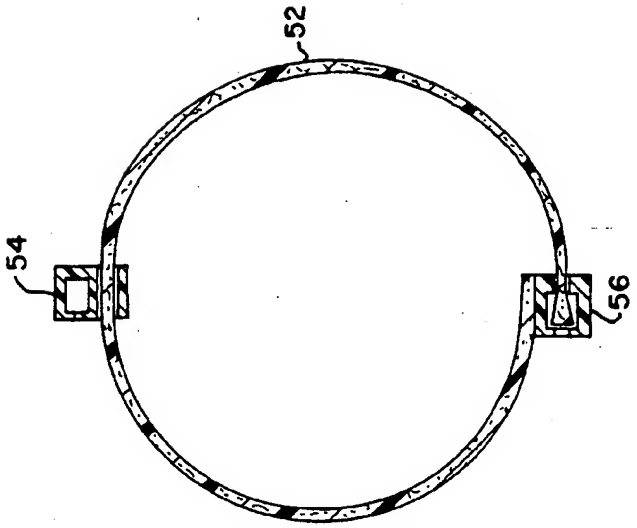


FIG. 11

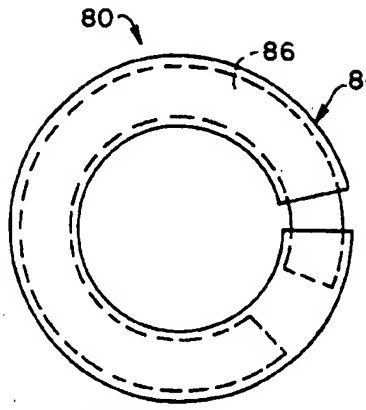


FIG. 15

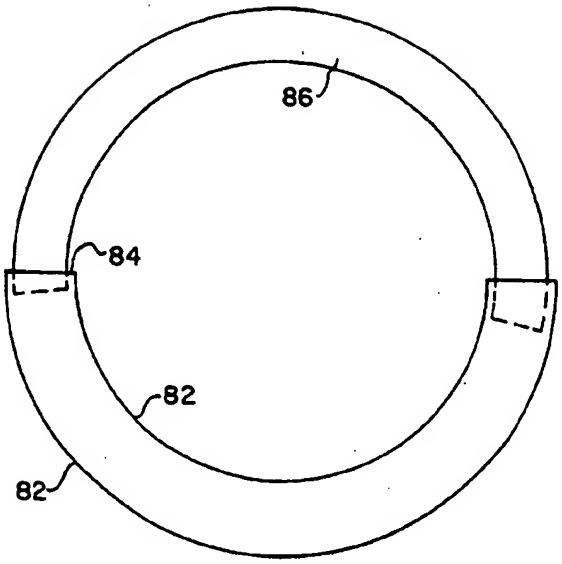


FIG. 16

FIG. 14

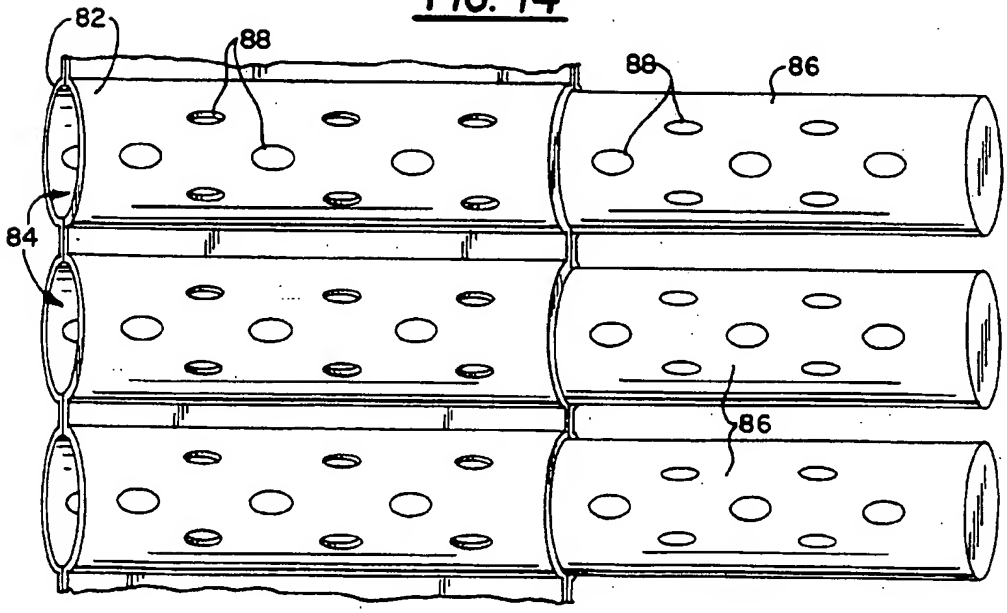


FIG. 18

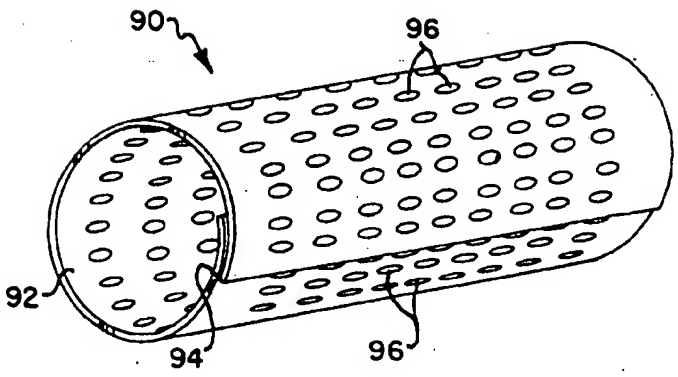
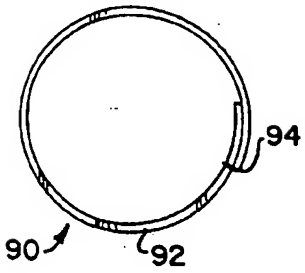


FIG. 17



BIOABSORBABLE STENT AND METHOD OF MAKING THE SAME

The invention described herein was made in the course of work under grant or award from the U.S. Department of Health and Human Services.

This is a continuation of application Ser. No. 07/701,154, filed May 17, 1991, now abandoned, which is a continuation-in-part of application Ser. No. 07/658,708, filed Feb. 21, 1991, now abandoned, which is a continuation-in-part of application Ser. No. 07/524,884, filed May 18, 1990, now abandoned, which is in turn a continuation-in-part of application Ser. No. 07/066,345, filed Jun. 25, 1987, now U.S. Pat. No. 5,059,211. application Ser. No. 07/701,154, is also a continuation-in-part of application Ser. No. 07/649,534, filed Feb. 1, 1991, now U.S. Pat. No. 5,306,286, which is a continuation of application Ser. No. 07/066,345, now U.S. Pat. No. 5,059,211, the disclosures of all of the listed applications being incorporated herein by reference.

BACKGROUND OF THE INVENTION

1. Field of the Invention

This invention relates to a stent for maintaining the patency of a body passage. In addition to maintaining patency, the stent can serve as drug delivery vehicle to effect localized pharmacologic therapy. The invention has particular application in the field of coronary angioplasty and will be described with reference thereto. In that realization the invention primarily relates to bioabsorbable (and thus biodegradable) stents for placement within a blood vessel, such as a coronary artery, to treat acute arterial closure and to prevent restenosis following angioplasty. However, the invention may also advantageously find application in dilating and maintaining the patency of other body passages, such as the ureters and the fallopian tubes.

2. Description of the Related Art

Coronary angioplasty typically involves the use of a catheter system including a dilation catheter which is introduced via the femoral artery under local anesthesia and is advanced to the site of a stenotic lesion in a coronary artery. The dilation catheter is for example a balloon catheter which is inflated with a fluid once it has been disposed within the targeted stenotic portion of the coronary artery. As the balloon is inflated, the atherosclerotic material along the vessel walls is compressed to thereby dilate the flow passage through the coronary artery.

While balloon angioplasty has become a relatively common and successful procedure, restenosis following angioplasty frequently occurs. Furthermore, the atherosclerotic plaque can crack during expansion which greatly increases the likelihood that the coronary artery will subsequently collapse.

It would therefore be desirable to avoid or minimize restenosis of a blood vessel, such as a coronary artery, by maintaining atherosclerotic plaque in its compressed disposition while at the same time preventing vessel collapse.

With the foregoing object, metallic stents have been developed and carried to stenotic portions of coronary arteries for placement after the vessel segment has been dilated by a balloon catheter or at the time of atherosclerotic plaque compression.

One such metallic stent has been proposed and tested in Europe and described in the article of Sigwart, et al titled "Intravascular Stent to Prevent Occlusion and Restenosis after Transluminal Angioplasty", published in the *New England Journal of Medicine*, Vol. 316, 12, Mar. 19, 1987, pp. 701–706. That stent is a metallic "Chinese finger handcuff" which can be expanded in diameter while simultaneously reduced in length and compressed in diameter while simultaneously elongated. The stent remains in its distorted configuration after the distorting force is removed.

The metallic stent is made by cutting a desired length from an elongated tube of metal mesh. As a result, it has the disadvantage that metal prongs from the length cutting process remain at the longitudinal ends of the stent. The inherent rigidity of the metal used to form the stent together with the terminal prongs make navigation of the blood vessels to the locus of the targeted stenotic lesion difficult as well as risky from the stand point of injury to healthy tissue along the passage to the target vessel. Further, once the stent has been permanently disposed within the target vessel, the beating of the patient's heart can cause the terminal prongs to damage the healthy vessel walls adjacent to the stenotic portion of the artery, even after endothelial encapsulation. This damage can lead to arterial rupture or aneurysm formation. Finally, because the metallic stent is intended to be chronically implanted within the vessel, continued exposure of the stent to blood can lead to undesirable thrombus formation within the blood vessel.

SUMMARY OF THE INVENTION

It would therefore be desirable to provide a stent for disposition within a blood vessel, such as a coronary artery, that has sufficient hoop strength to support the vessel wall against collapse and yet is flexible and compliant enough for safe and effective delivery to the site of a stenotic portion of a coronary artery. It would also be desirable to provide a stent which is soft and compliant to avoid arterial rupture or aneurysm formation at the ends of the stent even when exposed to continuous stresses from the beating heart following implantation.

It would be desirable, in the alternative to form such a stent as a sheet of preferably though not necessarily bioabsorbable material which has been rolled into a substantially cylindrical configuration and which has at least one of pores therein and apertures defined therethrough so as to allow endothelial cells to grow into and over the stent so that bioabsorption or degradation will occur within the vessel wall rather in the lumen of the vessel and further to allow blood flow through the stent where, for example, the stent traverses a branch of the blood vessel.

It would even further be desirable to provide a stent which avoids the limitations of chronic implantation by being absorbed into the blood vessel wall after healing of the angioplasty site. It would further be desirable to form such a bioabsorbable stent in a mesh-like or helical array of strands of biodegradable/bioabsorbable material which will enable endothelial cells at the angioplasty site to grow into and over the stent so that biodegradation will occur within the vessel wall rather than in the lumen of the vessel which could lead to embolization of the dissolved material.

A bioabsorbable stent is provided in accordance with the present invention which can support a vessel wall following coronary angioplasty but which overcomes the deficiencies of prior art metallic stents. More particularly, the present invention relates to a bioabsorbable stent for placement at the locus of, for example, a stenotic portion of a coronary artery which is flexible and compliant for safe and effective delivery to the targeted portion of the coronary artery and so as to avoid arterial rupture or aneurysm formation while

exposed to continuous stresses from the beating heart. The stent formed in accordance with the present invention can be a self-expanding stent formed from a plurality of strands of biodegradable material which can be deformed so as to have a reduced diameter which facilitates delivery of the stent to the targeted portion of a coronary artery and, once disposed at the target portion of the artery, can be allowed to expand to its preformed configuration to dilate and support that portion of the blood vessel. In the alternative, the stent formed in accordance with the present invention can be a sheet of bioabsorbable or biodegradable material which has been rolled in to a substantially cylindrical configuration which, through the memory of the material, will tend to expand in diameter when a force maintaining the same in a relatively reduced configuration is released.

The self-expanding stent provided in accordance with the present invention can be transported to a stenotic portion of an artery within a catheter which retains the same in its compact, reduced diameter configuration and then ejected from the catheter delivery system at the site of the stenotic lesion where it is allowed to return to its preformed configuration. In the alternative, the stent of the invention can be mounted to an expandable delivery device which maintains the stent in its reduced diameter configuration until deployment of the stent is desired. The forces maintaining the stent in its collapsed configuration are released to allow the stent to expand to its desired, preformed configuration. Expansion of the stent to its final configuration can be augmented and/or facilitated by, for example, inflating a balloon catheter therewithin to urge the stent into contact with the vessel walls to ensure maximal support of the blood vessel as well as prompt encapsulation of the stent structure. In that regard, where dilation of the stent is encouraged at the site of the stenotic lesion, plaque can be compressed at the time of stent placement rather than or in addition to prior dilation.

One skilled in the art will appreciate that a stent formed in accordance with the present invention can also be expandable from a reduced diameter configuration (as opposed to self-expanding). As such, the stent can be delivered to the locus of a lesion in a reduced diameter configuration on the distal end of an expandable catheter and can be expanded in vivo to its supporting diameter by expanding the expandable portion of its associated catheter. An expandable stent in accordance with the invention, may be a mesh type configuration or as detailed herein below may be advantageously in the form of a sheet of biocompatable and preferably bioabsorbable material. An expandable stent, in accordance with the invention, may also be formed from a plurality of sheets or strips of bioabsorbable material which are interconnected and wherein the means for interconnecting the strips of bioabsorbable material provide a means for retaining the stent in a reduced diameter configuration and a means for retaining the stent in its expanded or dilating configuration. The means for retaining the bioabsorbable stent in its reduced or expanded configuration, particularly where the stent is a sheet or segment of bioabsorbable material, can be merely the frictional forces between adjacent portions of the bioabsorbable sheet.

Other objects, features and characteristics of the present invention, as well as the methods of operation and functions of the related elements of the structure, and the combination of parts and economies of manufacture, will become more apparent upon consideration of the following detailed description with reference to the accompanying drawings, all of which form a part of this specification.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. **1** is an elevational view illustrating the delivery of a stent provided in accordance with the present invention to the site of a stenotic lesion within a coronary artery;

FIG. **2** is an enlarged elevational view of a stent provided in accordance with the present invention disposed within a catheter delivery system of the type illustrated in FIG. **1**;

FIG. **3** is an enlarged elevational view partly in cross-section showing the stent of the invention disposed within a targeted portion of a blood vessel, prior to disengagement from the delivery catheter assembly;

FIG. **4** is an enlarged elevational view similar to FIG. **3** but following disengagement from the delivery catheter assembly;

FIG. **5** is a perspective view of a stent formed in accordance with the present invention in its reduced diameter configuration mounted to the collapsed balloon of a balloon catheter;

FIG. **6** is a perspective view showing the stent of the invention following release and expansion of the stent upon expansion of the balloon catheter;

FIG. **7** is schematic perspective view showing a stent in accordance with an alternate embodiment of the invention;

FIG. **8** is a cross-sectional view of the stent of FIG. **7** in its reduced diameter configuration;

FIG. **9** is an enlarged view of portion A of FIG. **8**;

FIG. **10** is an enlarged view of portion B of FIG. **8**;

FIG. **11** is a cross-sectional view of the stent of FIG. **7** in its enlarged cross-sectional configuration;

FIG. **12** is an enlarged view of portion C of FIG. **11**;

FIG. **13** is an enlarged view of portion D of FIG. **11**;

FIG. **14** is a schematic perspective view of a further alternate embodiment of the invention;

FIG. **15** is a schematic end view showing the embodiment of FIG. **14** in its reduced diameter rolled configuration;

FIG. **16** is a schematic end view of the stent of FIG. **14** in its enlarged configuration;

FIG. **17** is a perspective view of yet a further alternate embodiment of the invention;

FIG. **18** is a schematic end view of the embodiment of FIG. **17**.

DETAILED DESCRIPTION OF THE PRESENTLY PREFERRED EXEMPLARY EMBODIMENTS

The stent to which the present invention relates can be either expandable or self-expanding in form. A detailed description of a stent of the self-expanding type is provided below. The self-expanding stent provided in accordance with the present invention can be woven from a plurality of strands of biodegradable material into a diamond-braided pattern. For example, the self-expanding stent can be woven from 8 strands of a bioabsorbable polymer. Thus the strands for forming the bioabsorbable stent are extruded, drawn and then braided to form the basic tubular stent. The stent is then cut to length and heat set. The severed ends of the stent are welded together by means of laser, heat, ultrasound or glue, for example. The stent so formed has memory characteristics such that if it is distorted in length and/or diameter, it will return or tend to return to its preformed configuration upon the release of external forces. Thus the stent is self-expanding when distorted so as to reduce the diameter thereof and subsequently released. Finally, the stent is formed from a material and braided such that the stent can withstand collapse pressures in excess of 200 mmHg.

In order to deliver the bioabsorbable stent **10** of the invention to the site of a stenotic lesion, it is necessary for the external diameter of the stent to be reduced so that the stent can easily traverse the blood vessels leading to a targeted portion of a coronary artery and disposed within the reduced diameter portion of the artery. Thus, the stent must be reduced by for example elongating the stent, allowing for a corresponding reduction in diameter, and maintained in such a reduced diameter or collapsed configuration during the delivery process. Once at the targeted portion of the coronary artery, the forces tending to reduce the diameter of the stent are released whereby the stent can support and/or dilate the stenotic portion of the coronary artery.

With reference to FIGS. **1** and **2**, the collapsed or reduced diameter bioabsorbable stent **10** in accordance with the present invention can be delivered to a targeted portion of a blood vessel by placing the reduced diameter stent within a delivery sheath **12** which is turn fed through a guide catheter **14** through the aorta **16** to the left or right coronary ostium. The stent carrying sheath **12** is then advanced from the distal end of the guide catheter **14** over a guide wire **18** into the targeted coronary artery and to the site of a stenotic lesion **20**.

A second sheath **22** is provided proximally of the collapsed stent **10** and is used to facilitate removal of the stent **10** from the outer sheath **12**. More particularly, with reference to FIGS. **3** and **4**, once the sheath **12** has been disposed at the targeted stenotic portion **20** of the coronary artery, the inner, proximal sheath **22** is held in place while the outer sheath is retracted or pulled proximally with respect to the stent **10**. Removal of the outer sheath **12** removes the forces which retain stent **10** in its collapsed configuration and thus allow the stent to self-expand within the stenotic portion **20** of the coronary artery to support and dilate the vessel walls (FIG. **4**). The inner sheath **22** prevents stent **10** from moving proximally with outer sheath **12**. The inner and outer sheaths **22, 12** as well as the guide wire **18** and guide catheter **14** can then be removed from the vascular system. In the alternative, the inner and outer sheaths can be removed and a balloon catheter (not shown in FIGS. **3** and **4**) fed through the guide catheter **14** over the guide wire **18** and into the expanded stent **10**. The balloon can then be inflated within the stent so as to urge the stent into firm engagement with the walls of the coronary artery and/or to augment the dilation of the artery effected by the stent alone.

With reference to FIGS. **5** and **6**, in the alternative, a bioabsorbable stent **10** formed in accordance with the present invention can be delivered to the site of a stenotic portion of a coronary artery on a balloon catheter **30**. More particularly, with reference to FIG. **4**, the stent **10** in its reduced diameter, slightly elongated configuration can be secured to the exterior surface of a collapsed balloon **32** provided on the end of a balloon catheter **30**. The stent **10** can be secured to the balloon with any suitable biocompatable glue or adhesive.

The balloon catheter **30** with stent **10** fixedly secured thereto is then fed over a guidewire **34** to the site of a stenotic portion of a blood vessel, such as a coronary artery. Once the balloon catheter **30** has been properly located, the distal balloon **32** is inflated. Inflation of the balloon **32** disengages the stent **10** from the exterior surface of the balloon by disturbing the points of adhesive securement between the stent **10** and the balloon **32**. Once the adhesive securement of the stent **10** has been released, the stent is free to and tends to resume its preformed configuration and thus re-expands or self-expands. Simultaneous inflation of the balloon **32** ensures that the self-expanding stent fully expands and is in supporting engagement with the blood vessel. In addition, the dilation or inflation of the balloon can simultaneously effect or encourage the dilation of the stenotic portion of the blood vessel. Thus, the balloon catheter **30** not only provides a delivery system for the stent of the invention but ensures that the stent is fully expanded once in place and can simultaneously dilate the targeted portion of the blood vessel.

In the alternative to providing a stent in the form of a mesh, whether self expanding or positively expandable, a stent in accordance with the invention may be formed as a sheet or plurality of sheets or strips of bioabsorbable material which are formed or are rolled so as to define a substantially cylindrical configuration for expanding and supporting walls of a body passage, such as a coronary artery. Thus, in the embodiment of the invention illustrated in particular in FIG. **7**, a stent **50** in accordance with the invention is in the form of a series of strips **52** of bioabsorbable material which are supported in predetermined spaced relation by first and second elongated supporting and fastening ribbons **54,56**. The ribbons, like the strips are bioabsorbable.

Ribbon **54** has a compartment **58** with an access opening **60**. A plurality of compartments **58** may be provided or a continuous compartment **58** with continuous or intermittent opening(s). Each strip **52** of bioabsorbable material has an enlarged longitudinal end or has a bulbous element mounted thereto so as to provide a relatively large longitudinal end **62**. As shown, the bulbous end **62** of each of bioabsorbable strip **52** has tapered walls so that it gradually increases in cross-section to facilitate passage of the bulbous portion **62** through the slit or slot **60** defined in the ribbon **54**, while preventing entry of the bioabsorbable strip in the reverse direction. Ribbon **54** further includes a plurality of transverse passages **64** through which each strip **52** of bioabsorbable material passes.

The second elongated ribbon **56** also defines a chamber **66** for receiving the bulbous portion **62** of the bioabsorbable strip(s) **52** and provides first and second passages **68,70** for each such receiving chamber **66**. The wall thickness of ribbon **56** differs on each side of the bulbous portion receiving chamber **66**. On one side, the wall has relatively thin wall portions **72** to allow deflection of the wall upon engagement of the inclined surfaces of the bulbous portion **62** of the bioabsorbable strip **52**. The other wall includes relatively thick wall portions **74** which do not deflect upon engagement with the inclined walls of the bulbous portion **62** and, thus, the bulbous portion which enters through the flexible walls **72** will be retained within the chamber **66** and cannot escape from the opposite side walls **74** of the chamber **66**. The opposite longitudinal end **76** of each bioabsorbable strip **52** is secured to the second ribbon **56** as shown in FIG. **10**. Any suitable means can be provided for such attachment but it is envisioned that such securement can best be provided with a biocompatable glue.

Prior to insertion of the bioabsorbable stent into the body passage, the stent is in a compacted configuration as illustrated in particular in FIG. **8**.

When the stent **50** illustrated in FIG. **8** is to be expanded within a desired portion of a stenotic body passage, such as a coronary artery, a force is applied from the radial center of the stent outwardly to expand the stent. This causes the bulbous portion **62** of the bioabsorbable sheets or strips **52** to be urged outwardly of the first ribbon **54** (to the left in FIG. **9**) and out of the bulbous portion receiving chamber **58**. At the same time, the bioabsorbable strip is fed through the

passage 64 in the first ribbon 54, to the left as shown in FIG. 9. Likewise, the bioabsorbable strip moves through the bulbous receiving chamber 66 in the second ribbon 56 (to the right as illustrated in FIG. 10). Ultimately, as shown in FIG. 11, the stent will have attained its maximal diameter at which time the bulbous portion 62 of the bioabsorbable strip 52 has deflected the walls 72 of the chamber 66 in the second ribbon 56 and entered that chamber, but is incapable of further passing through the chamber 66 by virtue of the relatively thick chamber walls 74. Thus, the stent 50 illustrated in FIG. 7 is retained in its reduced diameter configuration (FIG. 8) until a force is positively applied to the stent to enlarge it to its second configuration, shown in FIG. 11. Once the stent has been expanded, the bulbous portion 62 is captured in the second ribbon 56 and cannot exit that chamber 66 either back through the deflectable walls 72 or forwardly through walls 74 of that chamber. Thus, the stent will similarly be retained in it large diameter configuration.

Because the bioabsorbable strips are spaced apart along the length of the stent, blood can flow outwardly from within the stent to without, between the adjacent bioabsorbable strips and it is unnecessary to provide apertures allowing blood flow directly through the bioabsorbable stent material. However, such apertures can be provided and may be desirable to encourage tissue ingrowth. Otherwise, the strips of bioabsorbable material may advantageously have pores therein and/or apertures to allow both blood flow and tissue ingrowth. If the strips are sufficiently small in width, that is small in the dimension extended along the length of the stent, then such pores and/or apertures may be unnecessary.

As yet a further alternative, the bioabsorbable stent 80 formed in accordance with the present invention can be in the form of a pair of sheets 82 of bioabsorbable material which have been interconnected so as to define tine receiving cavities 84 with pieces of a solid bioabsorbable material in the form of plurality of tines 86 interconnected to the tine receiving cavities. Thus, the tine elements 86 are interconnected to first ends of the tine receiving cavities 84, as shown in FIG. 14, and the bioabsorbable structure can be rolled into a substantially cylindrical configuration with each tine element 86 inserted in the opposite end of the tine receiving cavity 84. To provide a bioabsorbable stent element in a substantially reduced configuration, the tine elements are inserted well into the tine receiving cavities as shown in FIG. 15. By suitably applying a expansion force to the interior of the reduced diameter stent, the tine elements 86 will slide relative to the bioabsorbable sheets 82 defining the tine receiving cavities 84 and thus enlarge the internal diameter of the stent as shown in FIG. 16. In accordance with this embodiment of the invention, the stent is retained in its reduced diameter configuration by the frictional interaction of the tine elements 86 and the tine receiving cavities 84. Likewise, in the enlarged configuration, frictional forces retain the tine elements 86 and tine receiving cavity portions 84 of the stent 80 in the desired orientation.

As schematically shown in FIG. 14, apertures 88 are defined both through the bioabsorbable sheets 82 defining the tine receiving cavities 84 and the tine elements 86 themselves so as to allow blood flow therethrough and/or endothelial tissue ingrowth. The bioabsorbable material itself which defines the tines and the tine receiving cavities can be porous to allow tissue ingrowth and/or to allow the incorporation of drugs therein as described more fully below. The apertures 88 schematically illustrated in FIG. 14 are for illustrative purposes only and the relative dimensions of the apertures 88 and the bioabsorbable material need not necessarily be as shown in that Figure.

In accordance with yet a further alternative embodiment of the invention as illustrated in particular in FIGS. 17 and 18, the stent 90 of the invention can be simply in the form of a rolled up sheet 92 of bioabsorbable material. Where the bioabsorbable material has shape retaining memory, the bioabsorbable material can be formed so as to be a roll of predetermined diameter which has been for example heat set. The stent is then forced, by further rolling the material, into a reduced diameter configuration which is maintained either by means of a buckle-like retention element 94 provided on the stent 90 itself or by capturing the stent 90 within or on a catheter element. When the force tending to maintain the stent in its reduced diameter configuration is released, then, the stent 90 will self expand to its original or close to its original diameter.

Where the stent is expandable, that is, one which retains substantially any shape into which it is distorted, the stent can be rolled into a reduced diameter configuration, which it retains naturally, and then, by applying an expanding force to the interior surface thereof, can be expanded to a desired diameter and will retain that substantially enlarged diameter upon the release of the expanding force.

As schematically illustrated in particular in FIG. 17, the bioabsorbable sheet 92 provided in accordance with this embodiment of the invention also has a plurality of pores and/or apertures 96 defined therethrough to allow blood flow through the stent 90 and/or tissue ingrowth for encapsulation. The bioabsorbable material can be porous and further can include apertures defined therethrough to enhance tissue encapsulation, bloodflow, therethrough and/or to provide cavities for receiving and carrying a drug to a targeted area of a body passage to be treated. In the alterative, as also detailed herein below, the material of the stent can have a drug incorporated therein when formed, which drugs will leach therefrom following placement in the body. The relative size of the apertures illustrated in particular in FIG. 17 is schematic and in actual practice, the pores or apertures through the stent may be larger or smaller then those illustrated.

As noted above, the stent formed in accordance with the present invention is preferably formed from a biodegradable polymeric material. The particular polymer selected and the thickness of the same, in particular, will determine the rates of biodegradation and bioabsorption and the structural characteristics of the stent during degradation and absorption should therefore be selected in accordance with the desired absorption period and characteristics of the stent.

Materials suitable for use in forming the bioabsorbable stents to which the invention relates are such that, when fabricated in the desired geometry, afford the stent sufficient strength to withstand collapse pressures of at least 100 mmHg, preferably at least 200 mmHg. Suitable materials do not produce toxic reactions, or act as carcinogens at the exposure levels present at the stent site. Suitable materials degrade and are absorbed with the production of physiologically acceptable breakdown products and the loss of strength and mass are appropriate to the particular biological environment and clinical function requirements.

In accordance with a preferred embodiment of the invention, the stent is formed of poly-L-lactide. Alternative preferred stent forming materials include copolymers of L-lactide with DL-lactide or D-lactide or glycolide, as well as homopolymers of beta-hydroxybutyric acid and its copolymers with other beta-hydroxy aliphatic acids. Polymers of omega hydroxy acids of the form $HO(CH_2)_nCO_2H$ where n is, preferably, 5–13 and polymers of aliphatic diacids and

diols of the form $HO_2C—(CH_2)_x—CO_2H$ and $HO—(CH_2)_y—OH$, where x is, preferably, 4–16 and y is, preferably, 2–18, can also be used to make stents characterized by varying rates of hydrolytic degradation.

Polyamides of the form $—NH—(CH_2)_n—CO—$ and $NH—(CH_2)_x—NH—CO—(CH_2)_y—CO—$, where n is, preferably, 6–13 and where x is, preferably, 6–12 and y is, preferably, 4–16, can also be used particularly where degradation slower than that achieved with poly-L-lactide is advantageous.

Polyanhydrides from diacids of the form $HO_2C—C_6H_4—O—(CH_2)_nOC_6H_4—CO_2H$, where n is, preferably, 2–8, give a range of values of Young's modulus and absorption rates, and copolymers of these with, for example, aliphatic alpha-omega diacids of up to about 12 carbon atoms can be used to provide stents having accelerated bioabsorption rates, advantageous in certain circumstances.

Polyorthoesters, such as are formed by the reaction of $(RO)_3C—X—C(OR)_3$ with $(HOCH_2)_2CH—Y—CH(CH_2OH)_2$, where R is an alkyl group, preferably a lower alkyl such as $CH_3—$ or $C_2H_5—$, X and Y are, for example, $—C_6H_4—$ or $—(CH_2)_n—$ where n is 1–12, or combinations of $—C_6H_4—$ and $—CH_2—$ groups, can also be used. Such polyorthoesters degrade in a biological environment to yield products that are bioabsorbed. One skilled in the art will appreciate that by varying R, X and Y, a range of hydrophobic character and Youngs modulus can be achieved thus providing stents of varying stiffness and biodegradability.

As indicated above, polylactide is a preferred material for stent formation. The hydrolysis of polyesters such as the polylactides is catalyzed by both acid and base. The pH of blood (7.3–7.4) is not sufficient to catalyze the hydrolysis. However, any hydrolysis taking place in the interior of the polymer will produce acidic breakdown products (lactic acid and its oligomers) that slowly diffuse and act as catalysts to autoaccelerate the degradation. The rate of degradation can be further accelerated, where desirable, by adding excipients such as citric acid or fumaric acid, or other relatively nontoxic acids during the polymer processing. The addition of acids is, preferably, carried out after the last heating during the polymer processing to minimize degradation of the polymers prior to implantation. For example, fumaric acid can be incorporated into a solution of poly-L-lactide (for example, a methylene chloride solution) prior to dry spinning. The solvent can be readily evaporated, for example, in warm air, and the fibers fabricated into stents and set in shape. A loading of 0.1–1.0% fumaric acid in the polymer is preferred. Shelf life of stents with acid excipients can be extended by keeping them dry and away from high temperatures.

Exposure to gamma radiation can also be used to effect chain scission with resulting formation of acid groups which accelerate stent degradation. The higher the dose, the more quickly the stent will degrade.

Other additives that can be used to accelerate stent degradation and thus absorption are substances that are not themselves an acid but which hydrolyze to produce an acid more rapidly than the polymer. An example is the tert. butyl ester of an acid, such as lauric acid or ditert. butyl fumarate. Such additives break down in warm, wet acidic environments, so that once in vivo degradation is initiated, catalysts are generated that further accelerate degradation.

The same principles used to design additives that accelerate degradation of the polymer in vivo can also be used to make comonomers for use with lactide which accelerate degradation. For example, a low molecular weight polymer of tartaric acid can be made by treating tartaric acid with ethyl ortho acetate, evaporating off ethyl alcohol and ethyl acetate. This low molecular weight polyester which can contain a few ortho ester units can be incorporated into lactide and subjected to polymerizing conditions to give a lactide/tartrate copolymer with hydrolyzable groups which produce carboxylic acids. One skilled in the art will appreciate that there are a large number of such possible comonomers as well as polymer additives. Preferred are those that do not produce significant inflammatory or toxic reactions when used in vivo and those that give desired reproducible rates of degradation and absorption when used in vivo.

Comonomers or additives that give a buffering effect upon hydrolysis can be used to retard biodegradation when a slower degrading material is desired. For example, a small amount (about 1–5%) of alanine copolymerized with lactide can be used to retard biodegradation. Other amino acids can be incorporated via copolymerization to give segments such as $—NH—(CH_2)_n—CO—$ where n=1–17, preferably, 1 and 5–10, in order to retard degradation.

The non-limiting Example that follows describes the use of melt spinning in the stent preparation process. One skilled in the art will appreciate that melt spinning lowers the molecular weight. That is, the molecular weight achieved during polymerization is reduced, fairly rapidly, when the polymer is melted. Higher molecular weight in the final product can be advantageous in that it gives: i) increased strength and toughness; ii) improved elastic recovery after deformation; and iii) a reduced rate of degradation and absorption.

Spinning from solution can be used in lieu of high temperature (about 190° C.) melt extrusion. Methylene chloride (b.p. 55° C.) is a preferred solvent for use in such a process. The solvent can be removed during the spinning process by: i) evaporating solvent from the protofibers descending from a spinneret with warm air (known in the art as dry spinning), or ii) squirting the polymer solution into a liquid bath, the liquid being a non-solvent for the polymer but miscible with the solvent in the spinning solution, e.g. methyl alcohol (known in the art as wet spinning).

The stents to which the invention relates can have incorporated therein, or coated thereon, one or more drugs, such as smooth muscle cell inhibitors (for example, growth factor inhibitors or cytotonic agents) collagen inhibitors, vasodilators (for example, prostaglandins or analogs thereof), or anti-platelet and/or anti-thrombotic substances (for example, aspirin, heparin or tissue plasminogen activator). (Imaging agents, such as radio-opaque fillers can also be used, as can agents that improve streamlined blood flow, such as hydrogels.) Such stents are excellent drug delivery vehicles as they can be used to achieve high local drug concentrations directly at the area at risk, for example, for restenosis, while at the same time avoiding problems associated with systemic drug administration, for example, toxicity. Timed release of the drug from the stent can be achieved either by forming the stent so that slow diffusion from the stent-forming polymer itself is effected or by coating the stent in a manner such that slow diffusion of the drug through, or from, the coating is effected.

In a preferred embodiment, the outer portion of the stent (the "skin") is made porous after the stent has been fabricated to accommodate the drug. The pores can be filled with a drug/gel forming matrix by alternating vacuum and hydrostatic pressure (for example, up to 6,000–20,000 psi). If necessary, the stent can then be contacted with a reagent that causes the matrix to set as a gel.

The porous skin can be formed by dipping the stent, or filaments from which the stent is to be formed, into a solvent that swells the outer layer of the filaments. Ideally, diffusion of the solvent is effected fairly slowly; diffusion can be slowed, for example, by chilling the solvent. In this way the core of the filament is not affected during the time of exposure to solvent. The filament with swollen outer layer can then be dipped into an agent that is a "nonsolvent" for the polymer of which the filaments are made, which agent forms a solution with the swelling solvent. This agent, preferably, diffuses more rapidly than the first solvent. Warming can be used to promote diffusion of the agent into the swollen area thus causing phase separation that results in the formation of a porous skin on the stent filament. If poly-L-lactide is used as the polymer, chloroform can be used as the swelling solvent and methyl alcohol as the agent that causes phase separation. Pore formation can also be effected in polylactic/glycolic acid polymers and copolymers using a blend of, for example, orthoesters (such as a methyl or ethyl orthoformate or orthoacetate) and methylene chloride as solvent and water as nonsolvent. The change in CED of the orthoester/water reaction product can be expected to produce phase separation and the molecular weight of the orthoester will produce a low rate of diffusion out of the solvent. If nylon 6/6 is used as the polymer, 75% aqueous formic acid can be used as the swelling solvent and 5% aqueous formic acid as the phase separation agent. Other suitable polymer/solvent/agent combinations can also be used. One skilled in the art can readily determine appropriate solvents/agents to be used with any particular polymer.

An example of a suitable gelling system includes a mixture of sodium alginate and neutral heparin. After this is introduced into the pores, the filaments can be dipped in aqueous calcium chloride which causes the alginate to gel.

As indicated above drugs to be delivered can be incorporated into the stent. The manner in which the drug is incorporated depends on the spinning technology used (melt spinning, dry spinning or wet spinning). (See, generally, Rodriquiz.)

One skilled in the art will appreciate that, as melt spinning involves the heating of the polymer above its melting point, the range of drugs that can be used in conjunction with this method is somewhat limited. Drugs that are sufficiently stable and unreactive at the high temperatures involved can, however, be blended with the polymer prior to extrusion.

In dry spinning, the polymer is dissolved in a solvent and the solution is extruded, the solvent being removed by warm air. The same analysis applies as in melt spinning but the temperatures can be substantially lower, increasing the number of drugs that can be incorporated.

In wet spinning, the polymer is dissolved in a solvent and extruded into a second liquid that is a "nonsolvent" for the polymer but which will extract the solvent for the polymer and coagulate the fibers. The analysis for this process is the same as for the development of porous skin discussed above with respect to the relative diffussivities of the two liquids, but wet spinning gives pores throughout the fiber diameter. Drug can be incorporated by running the fibers through a bath post-congulation, and rinsing. The pores can then be partially collapsed by stretching, heating, or solvent exposure thereby trapping the drug throughout the filament. If a heat sensitive drug is incorporated, then subsequent processing steps used must avoid high temperature, e.g., the heat setting step can be replaced by chemical setting (see below).

Other methods can also be used to incorporate drugs into the stents of the present invention. For example, small water soluble particulates can be added to the polymer before extrusion and leached out post-fabrication to create pores. Monomeric lactide can be incorporated before extrusion and subsequently leached out. Very small pores can be created by swelling the polymer at any stage post-extrusion in a supercritical fluid such as propane and then reducing the pressure so that no liquid phase exists. In all cases, drug containing solutions can be forced into the pores by hydrostatic pressure with or without a gelling agent to control out-diffusion of the drug.

One skilled in the art will appreciate from the foregoing that the stent to which the invention relates can be used as a vehicle for delivering virtually any drug. Care must be taken, however, to ensure that the fabrication process, particularly in those situations where the drug is to be incorporated into the stent, is selected such that the activity of the drug to be delivered is not diminished or destroyed. In addition to use of the spinning technologies noted above, the temperature of the setting step of stent formation must also be considered. As an alternative to annealing, which involves heating to temperatures in the range of 110°–140° C., chemical setting can be used. Specifically, the stent can be exposed to vapors or liquid of a poor solvent or weak swelling agent such as ethyl acetate, then air or vacuum drying to remove the solvent/agent (0°–40° C.).

Drugs particularly sensitive to thermal deactivation (for example, proteins, including tissue plasminogen activator) are preferably incorporated into a porous skin formed on the stent, as described above. Sterilization of the stent in the case of such drugs can be effected using gamma radiation.

One skilled in the art will recognize that the amount of drug to be incorporated into, or coated on, the stent will depend on the therapy sought. Such determinations can be made without undue experimentation.

From a reading of the following non-limiting Example, one skilled in the art will appreciate that variations in molecular weights, dimensions, draw ratios, temperatures and solvents are all possible without substantially altering the product stent.

EXAMPLE

Stent Preparation

Rectangular or cylindrical monofilaments made by melt extrusion of poly-L-lactide with an average weight of 35,000 daltons were drawn to 600% of their original length to give a final diameter for the cylindrical filaments of 0.18 mm. These fibers were braided onto a 4- to 8-foot Teflon mandrel, 3.17 mm in diameter, using 8 ends in the braiding process (four filaments moving in clockwise and four in counterclockwise helices, each filament alternately going over and under the intersecting filaments). The filaments were then secured to the mandrel with two wire twists at intervals such that each interval was slightly longer than the desired stent (typically, 0.5–2.0 cm in length). The spacing of the two wire twists was such that after annealing the mandrel and fiber could be cut between the wires to give a single stent length while constraining the fibers form shrinking during annealing. (The purpose of annealing is to heat set the fibers so they will return to a helical form if distorted after annealing.) The annealing was carried out at 140° C. for 15 minutes. (Higher temperatures (below the melting point) allow shorter annealing cycles and lower temperatures down to about 110° work better with longer times.) The annealing was done in air although an inert atmosphere such

as nitrogen or vacuum annealing result in somewhat higher molecular weight products.

The filaments of the partially formed stents were glued together at the desired terminal intersections, thereby determining the final length, with a small drop of a solution of poly-L-lactide in a volatile solvent such as chloroform, and removed from the mandrel. When the solvent has substantially evaporated, the stents are trimmed to remove most of the fibers beyond the glue joints and each joint is brought into proximity with a hot wire causing the ends to fuse and become smooth.

While the invention has been described in connection with what is presently considered to be the most practical and preferred embodiment, it is to be understood that the invention is not to be limited to the disclosed embodiment, but, on the contrary, is intended to cover various modifications and equivalent arrangement included within the spirit and scope of the appended claims. For example the preformed stent need not be a right cylinder but could have a cross-section which varies along the length of the stent. Further, solvent setting can be used in lieu of thermal annealing. Solvent setting is particularly advantageous where drugs are to be incorporated into the stent. In addition, the self expanding stent of the invention could advantageously be used in body passages other than the coronary arteries, such as the ureters or the fallopian tubes, such alternative applications and configurations being limited only by the appended claims.

What is claimed is:

1. A method of forming pores on the surface of a stent, the stent including a tubular main body portion having a first end, a second end, and a flow passage defined therethrough from said first end to said second end, said tubular main body portion being sized for intraluminal placement within a body passage, said main body portion being one of porous and apertured, at least in part, said main body portion being one of expandable and self-expanding from a first, reduced cross-sectional dimension to a second enlarged cross-sectional dimension whereby said main body portion can be transported intraluminally to a targeted portion of a body passage and expanded to a second enlarged diameter so as to engage and support said targeted portion of said body passage, the method comprising the steps of:

i) contacting material from which said stent is formed with a solvent that swells said material under conditions such that swelling of an outer layer of said material is effected; and

ii) contacting said material resulting from step (i) with an agent that is a nonsolvent for said material, which agent forms a solution with said solvent, under conditions such that said agent diffuses into said swollen outer layer of said material thereby causing phase separation and pore formation in said outer layer of said material.

2. The method according to claim 1, wherein said pores are formed in said outer layer of said material prior to formation of said stent from said material.

3. The method according to claim 1, wherein said pores are formed in said outer layer of said material after formation of said stent from said material.

4. The method according to claim 1, wherein said main body portion is formed at least in part from a bioabsorbable material.

5. A method of incorporating a drug into a stent, the stent including a tubular main body portion having a first end, a second end, and a flow passage defined therethrough from said first end to said second end, said tubular main body portion being sized for intraluminal placement within a body passage, said main body portion being one of porous and apertured, at least in part, said main body portion being one of expandable and self-expanding from a first, reduced cross-sectional dimension to a second enlarged cross-sectional dimension whereby said main body portion can be transported intraluminally to a targeted portion of a body passage and expanded to a second enlarged diameter so as to engage and support said targeted portion of said body passage, said stent having a therapeutically effective amount of a drug coated thereon or incorporated therewithin, the method comprising the steps of:

i) forming pores in an outer layer of material from which said stent is formed;

ii) introducing into said pores a composition comprising said drug and a gel forming agent; and

iii) effecting setting of said composition as a gel.

6. The method according to claim 5, wherein said main body portion is formed at least in part from a bioabsorbable material.

7. An intraluminal stent comprising a tubular main body portion having a first end, a second end, and a flow passage defined therethrough from said first end to said second end, said tubular main body portion being sized for intraluminal placement within a body passage, said main body portion being formed at least in part from a material which has been rolled into a substantially cylindrical configuration and thereby said main body portion has a central axis, said main body portion being one of porous and apertured with a plurality of apertures, at least in part, said main body portion being expandable from a first, reduced cross-sectional dimension to a second enlarged cross-sectional dimension whereby said main body portion can be transported intraluminally to a targeted portion of a body passage and then can be expanded to said second enlarged cross-sectional dimension so as to engage and support said targeted portion of said body passage, said main body portion including means for retaining said main body portion in said reduced cross-sectional configuration and means for retaining said main body portion in said enlarged cross-sectional configuration, said main body portion being in the form of at least one strip of material, said means for retaining comprising an elongated connector element provided adjacent a first end of said strip of material, said connector element having a radially inner wall and a radially outer wall defining therebetween a strip receiving passage extending in a first direction from a first open end to a second end thereof, said strip receiving passage extending in said first direction at least part circumferentially of said main body portion, said strip of material being slidably disposed in said strip receiving passage whereby sliding movement of said strip of material in said first direction decreases a diameter of said main body portion and sliding movement of said strip of material in a second direction, opposite to said first direction, increases a diameter of said main body portion, at least a portion of said strip of material being disposed in said passage when said main body portion has said first cross-sectional dimension and at least a portion of said strip of material being disposed in said passage when said main body portion has said second cross-sectional dimension, wherein said second end of said passage is open, and said strip of material extends through said passage to selectively protrude from said first and second open ends thereof.

8. A stent as in claim 7, wherein said means for retaining comprises frictional engagement between said strip of material and said connector element.

9. A stent as in claim 7, wherein first and second connector elements are provided, one of said connector elements being fixedly secured to said first end of said strip of material.

10. A stent as in claim 9, wherein each of said connector elements includes means for slidably receiving said strip of material.

11. A stent as in claim 7, wherein a plurality of strips of material are provided.

12. The stent according to claim 7, wherein said main body portion is formed at least in part from a bioabsorbable material.

13. The stent according to claim 7, wherein said main body portion has a therapeutically effective amount of a drug coated thereon or incorporated therewithin.

14. An intraluminal stent comprising a tubular main body portion having a first end, a second end, and a flow passage defined therethrough from said first end to said second end, said tubular main body portion being sized for intraluminal placement within a body passage, said main body portion being formed at least in part from a material which has been rolled into a substantially cylindrical configuration and thereby said main body portion has a central axis, said main body portion being one of porous and apertured, at least in part, said main body portion being expandable from a first, reduced cross-sectional dimension to a second enlarged cross-sectional dimension whereby said main body portion can be transported intraluminally to a targeted portion of a body passage and then can be expanded to a second enlarged diameter so as to engage and support said targeted portion of said body passage, said main body portion including means for retaining said main body portion in said reduced diameter configuration and means for retaining said main body portion in said enlarged diameter configuration,

said main body portion including a plurality of tine receiving cavities and a plurality of tine elements, said tine receiving cavities each extending in a first direction at least part circumferentially of said main body portion from a first open end to a second end thereof, said tine elements being slidable in respective tine receiving cavities whereby sliding movement of said tine elements in said first direction in said tine receiving cavities selectively increases or decreases a diameter of said main body portion.

* * * * *

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(12) **United States Patent**
Randall et al.

(10) **Patent No.: US 6,190,590 B1**
(45) **Date of Patent: Feb. 20, 2001**

(54) **APPARATUS AND METHOD FOR MAKING FLANGED GRAFT FOR END-TO-SIDE ANASTOMOSIS**

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(73) Assignee: **Impra, Inc.**, Tempe, AZ (US)

(*) Notice: Under 35 U.S.C. 154(b), the term of this patent shall be extended for 0 days.

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§ 371 Date: **Aug. 27, 1998**

§ 102(e) Date: **Aug. 27, 1998**

(87) PCT Pub. No.: **WO97/31590**

PCT Pub. Date: **Sep. 4, 1997**

(51) **Int. Cl.**[7] **B29C 33/30**; B29C 49/44; B29C 55/24; B29C 69/02; B29D 23/00

(52) **U.S. Cl.** **264/138**; 264/151; 264/159; 264/296; 264/314; 264/320; 264/523; 264/540; 264/573; 264/536; 264/138; 425/182; 425/185; 425/195; 425/389; 425/392; 425/393; 425/527; 425/531; 623/1; 623/11; 623/12

(58) **Field of Search** 264/101, 151, 264/159, 296, 320, 314, 523, 536, 540, 571, 573; 425/185, 195, 392, 393, 387.1, 388, 389, 522, 527, 531, 182; 623/1, 11, 12

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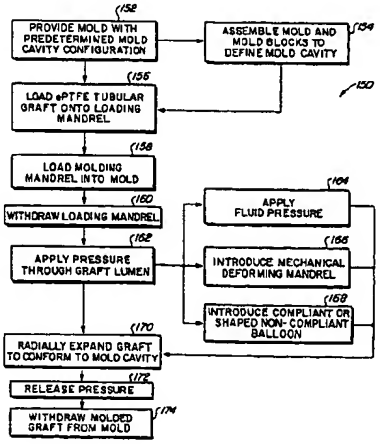
Primary Examiner—Jan H. Silbaugh
Assistant Examiner—Michael I. Poe
(74) *Attorney, Agent, or Firm*—Morrison & Foerster LLP; Todd W. Wight

(57) **ABSTRACT**

A method and apparatus for forming a flanged polytetrafluoroethylene cuffed section from a tubular polytetrafluoroethylene graft. The flanged polytetrafluoroethylene graft is well suited for use as a distal bypass graft, for arteriovenous grafting, or as a hemodialysis access graft. The graft includes an integral terminal polytetrafluoroethylene flanged skirt or cuff section which facilitates an end-to-side anastomosis directly between an artery and the polytetrafluoroethylene flanged graft without need for an intervening venous collar or venous patch.

19 Claims, 4 Drawing Sheets



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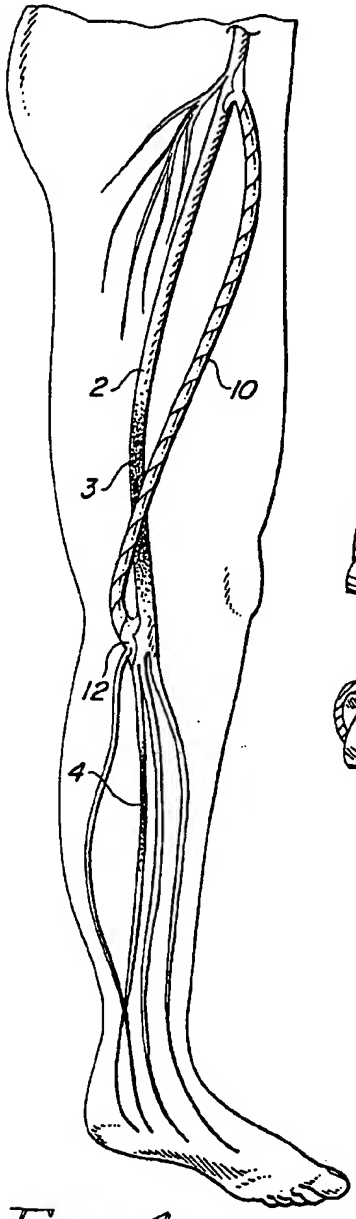


FIG. 1

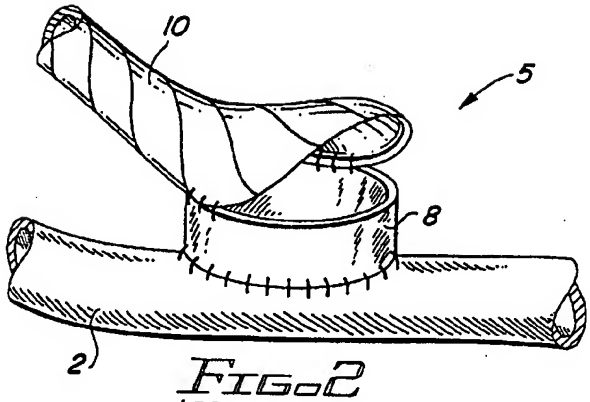


FIG. 2
(PRIOR ART)

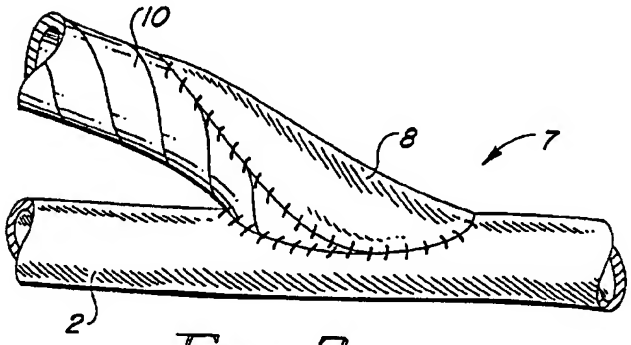


FIG. 3
(PRIOR ART)

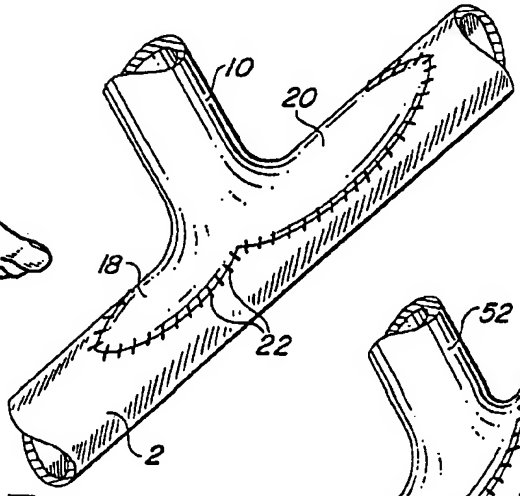


FIG. 4B

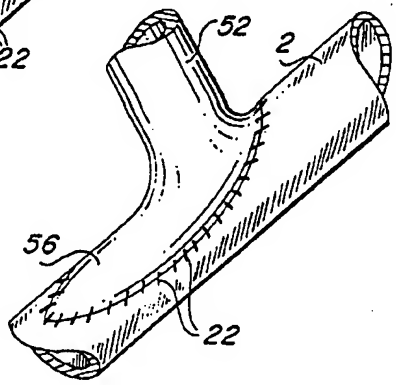


FIG. 6B

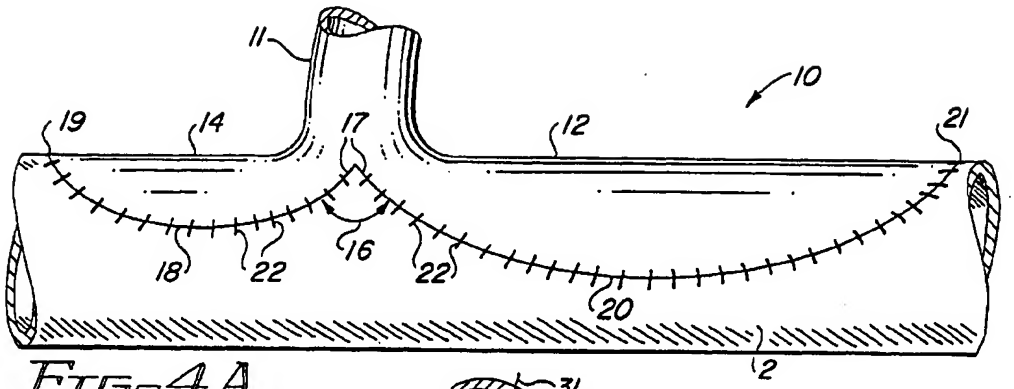


FIG. 4A

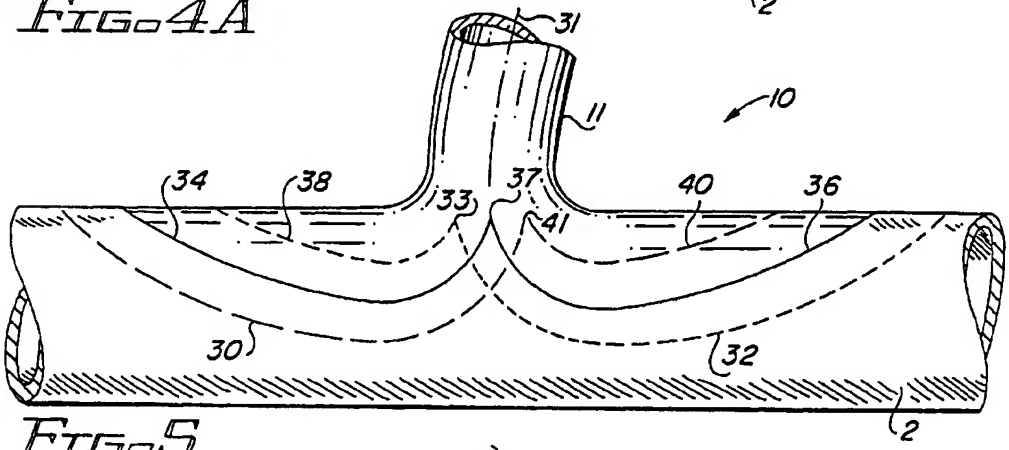


FIG. 5

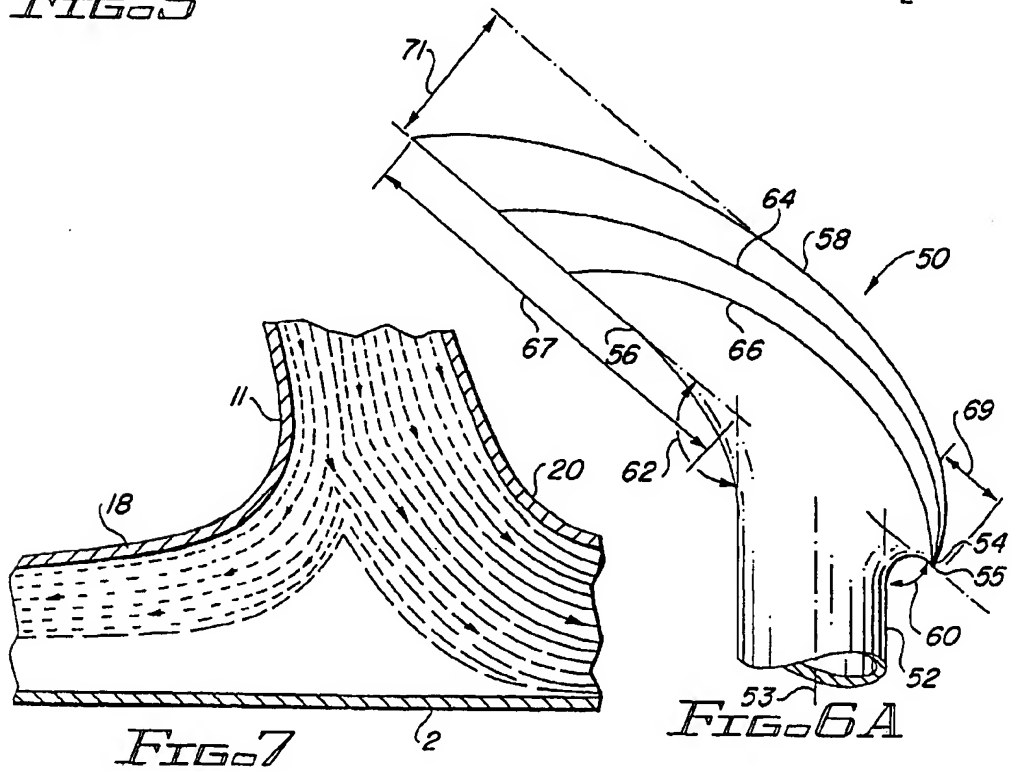
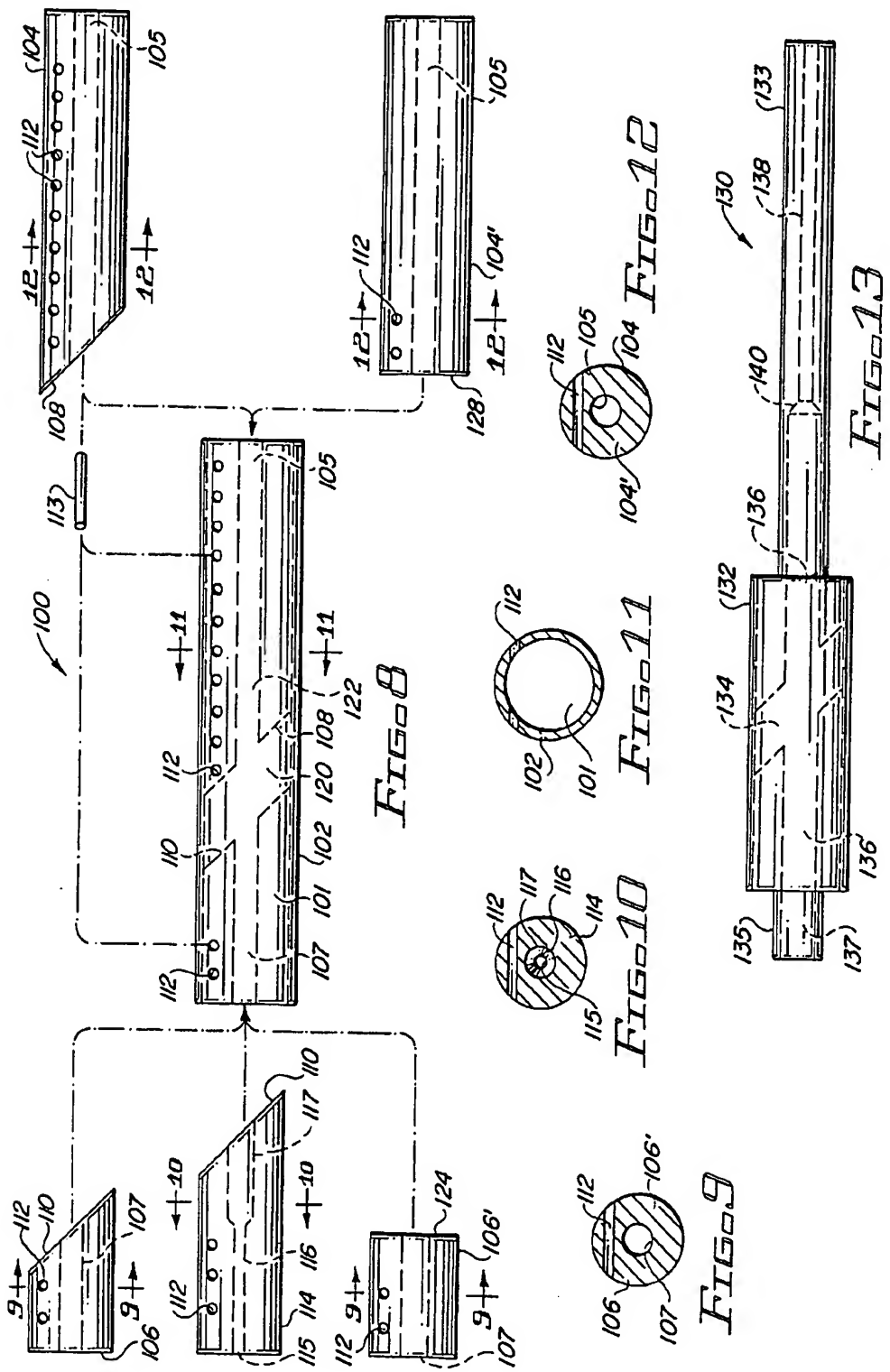


FIG. 7

FIG. 6A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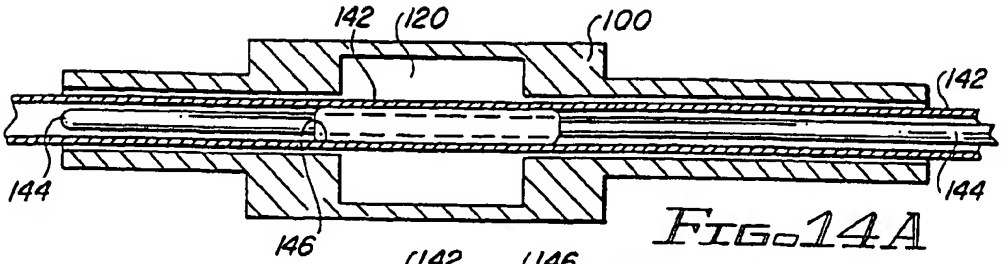


FIG. 14A

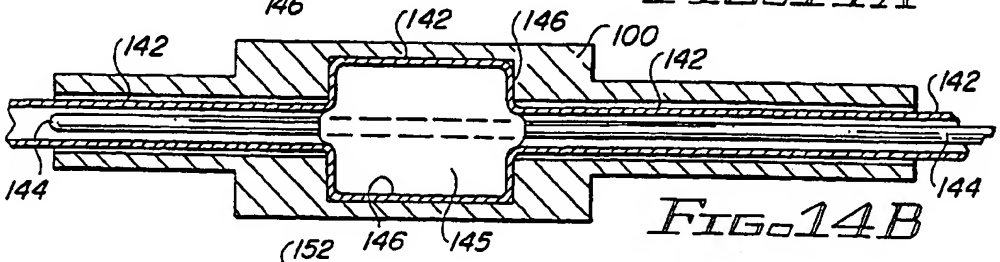


FIG. 14B

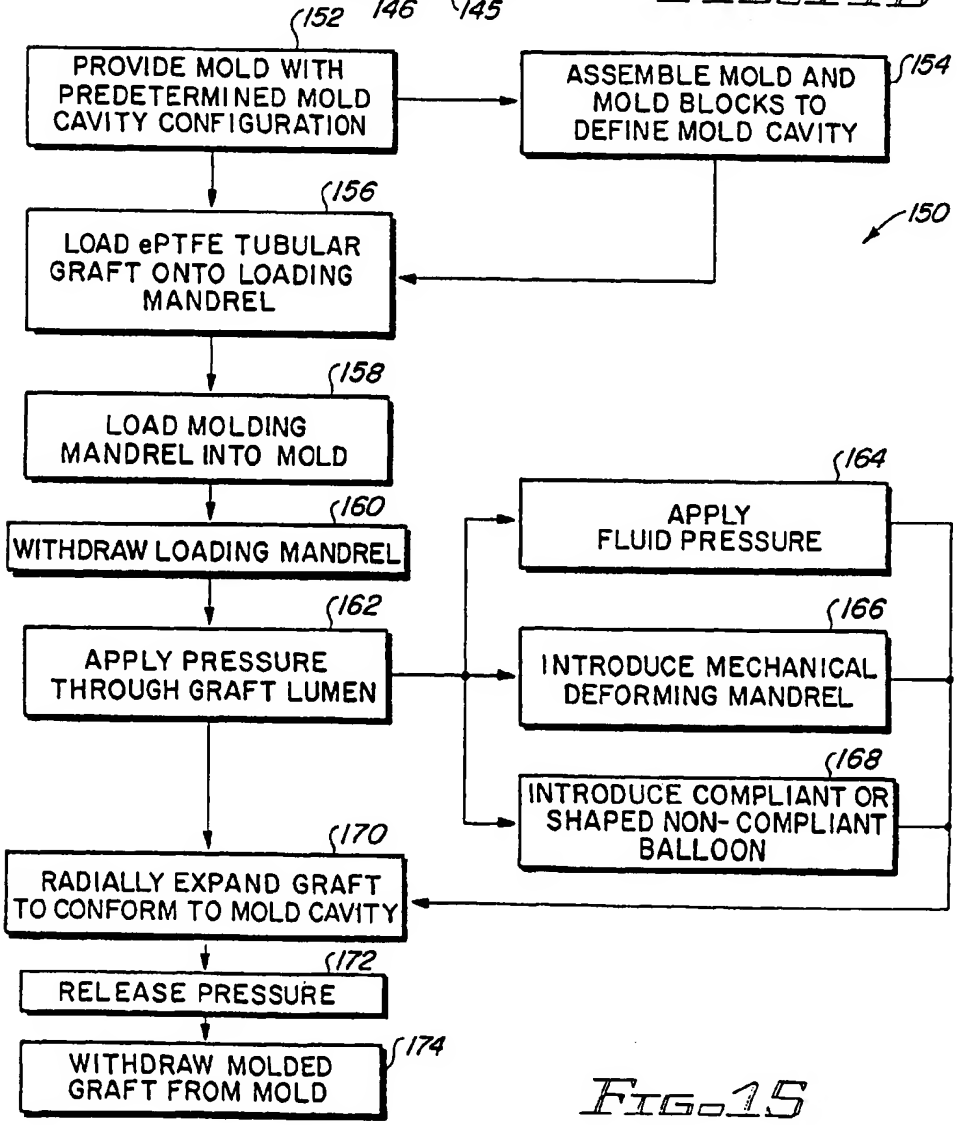


FIG. 15

APPARATUS AND METHOD FOR MAKING FLANGED GRAFT FOR END-TO-SIDE ANASTOMOSIS

CROSS-REFERENCE TO RELATED APPLICATIONS

This application is related to a PCT International Application PCT/US96/02714, which was concurrently filed with the United States Patent and Trademark Office acting as the International Receiving Office under the Patent Cooperation Treaty, entitled "Flanged Graft for End-to-Side Anastomosis," now U.S. Ser. No. 09/125,907. U.S. Ser. No. 09/125,907 is commonly assigned to IMPRA, Inc., the Applicant hereof who hereby expressly incorporates U.S. Ser. No. 09/125,907 by reference thereto as further denoted herein.

BACKGROUND OF THE INVENTION

1. Field of the Invention

The present invention relates generally to vascular grafts, and more particularly to a method and apparatus for forming the flanged polytetrafluoroethylene (PTFE) cuffed section from a tubular PTFE graft to form a flanged vascular graft for end-to-side anastomosis useful for purposes of bypassing an occluded or diseased section of a blood vessel or as an access graft for hemodialysis. The PTFE graft has an integral terminal PTFE flanged cuff section which permits an end-to-side anastomosis with a blood vessel in which the terminal PTFE flanged cuff section is sutured to the blood vessel and provides a PTFE-tissue interface between the graft and the blood vessel. The flanged PTFE graft is the subject of U.S. Ser. No. 09/125,907, which is hereby expressly incorporated by reference as being illustrative of types of flanged grafts useful for distal bypass or hemodialysis access grafts which may be made using the apparatus and method of the present invention.

2. Description of the Prior Art

The uses of cuff grafts for bypassing peripheral vascular occlusive conditions, particularly femoro-crural patch prostheses, or for hemodialysis access grafts are well known in the art. To date, however, either autologous grafts or synthetic grafts with a terminal cuff fashioned from venous tissue at the anastomotic site have been used. Examples of conventional cuffed grafts are the Miller collar described in J. H. Miller, *The Use of the Vein Cuff and PTFE*, in VASCULAR SURGICAL TECHNIQUES 2 ed., 276–286 (W. B. Saunders 1989), and the Taylor patch described in Taylor, R. S., et al, Improved technique for polytetrafluoroethylene bypass grafting: long-term results using anastomotic vein patches, *Br. J. Surg.*, 79:348–354 (1992). Both the Miller graft and the Taylor graft are cuff grafts and each employs a PTFE graft with an autologous venous cuff at the anastomotic site. The Miller collar and the Taylor patch each use venous tissue at the anastomotic site to avoid a compliance mismatch at the PTFE-tissue interface.

The flanged PTFE graft in U.S. Ser. No. 09/125,907, hereby incorporated by reference, offers a new type of anastomosis for femoro-crural bypass or access grafting in which the graft is fabricated in a flared, double-bulb configuration. The inventive graft configuration offers an optimal geometry for the anastomosis as a function of hemodynamic properties. By optimizing blood flow from the bypass prosthesis to the artery, formation of intimal hyperplasia may be reduced with a concomitant increase in graft patency and decreased morbidity.

The apparatus of the present invention consists of an annular mold having a radially extending annular slot, forming an expansion port. The flanged cuff graft is made by first forming an unsintered tubular PTFE vascular graft by extruding a PTFE lubricant mixture into a billet to form a tubular extrudate, placing the extrudate in the annular mold, and forming an annular cuff by either: 1) application of a negative pressure to the expansion port, or 2) application of positive pressure, as by a highly compliant angioplasty balloon, through the tubular extrudate lumen, to radially displace a section of the tubular extrudate, thereby forming a cuffed graft.

Various different approaches have been taken to fabricate branched grafts. As early as 1938, U.S. Pat. No. 2,127,903 to Bowen disclosed a bioabsorbable surgically implantable graft made of animal tissue and a binder formed by wrapping strips of the treated animal tissue about a structural form. U.S. Pat. No. 4,909,979, issued Mar. 20, 1990 to Possis, discloses a method of shaping a human umbilical cord for use as a vascular graft. The method employs a mandrel to support and shape the umbilical cord during forming and curing of the cord. The forming and curing process provides a cord with a blood flow restrictor section. PTFE coatings are provided on the mandrel to facilitate mounting the umbilical cord onto the mandrel. A shaping section of the mandrel is provided with a plurality of vacuum openings in the mandrel. The umbilical cord is treated with ethanol and a vacuum applied until the cord is dehydrated. The cord is then exposed to a curative and fixative solution and a vacuum applied until the umbilical cord is cured substantially airtight and circumferentially compressed and compacted around the mandrel forming section.

U.S. Pat. No. 4,354,495, issued Oct.19, 1982 to Bodicky, discloses a method of connecting a PTFE tube to a hub made of a moldable plastic, e.g., polyurethane, acrylics, polyethylene, polycarbonates, etc. The method involves selectively heating a portion of the PTFE tube to form a bulge or protrusion, then inserting the bulge into a mold and molding the moldable plastic hub about the bulge in the mold. U.S. Pat. No. 4,957,508, issued Sep.18, 1990 to Kaneko et al., discloses an elastomeric medical tube having proximal and distal ends, outwardly flared. The outward flare of the ends is achieved by forming the inner and outer surfaces of the tube to exhibit inverse elastomeric properties, i.e., the inner surface exhibits a dilating force, while the outer surface exhibits a shrinking force. The tube is made of high molecular weight polymers, particularly, polyvinyl halide, polystyrene, polyolefin series polymers, polyester series condensates, cellulose series high polymers, polyurethane series high polymers, polysulfone series resins, polyamides, etc. along with copolymers or mixtures of these.

U.S. Pat. No. 5,387,236 to Noshiki et al., issued Feb. 7, 1995, discloses a vascular prosthesis and method of making a vascular prosthesis by providing a vascular prosthesis substrate made of PTFE or other microporous material, and depositing and capturing within the wall of the prosthesis substrate fragments of biological tissue. The biological tissue fragments may be vascular tissues, connective tissues, fat tissues and muscular tissues and/or vascular endothelial cells, smooth muscle cells and fibroblast cells. The impregnation process is conducted by depositing the cellular material on the inner wall of the graft and applying a pressure differential between the lumenal and ablumenal wall surfaces to drive the tissue fragments into the microporous matrix of the vascular prosthesis. U.S. Pat. No. 4,883,453 to Berry et al., issued Nov. 28, 1989, discloses an aorto-coronary bypass graft and a method of making the graft. The graft consists of a plate portion and at least one tube portion

extending from the plate portion. The graft and plate are disclosed as being made of an electrostatically-spun fibrous structure. The graft is adhered to the plate by mounting the graft onto a mandrel, applying adhesive to the surface of the plate surrounding an opening in the plate, and passing the mandrel through an opening in the plate until the graft contacts the adhesive. The adhesive is any suitable adhesive for the materials forming the plate and the graft. According to the preferred embodiment described in this reference, the graft preferably has a tapered wall thickness, such that the graft wall thickness adjacent the plate is greater than that distant the plate.

U.S. Pat. No. 5,110,526 to Hayashi et al., issued May 5, 1992, discloses a process for producing molded PTFE articles. According to this process, unsintered PTFE extrudates are inserted into a sintering mold. The sintering mold has a diameter slightly larger than the outside diameter of the unsintered PTFE extrudate. Clearance between the outside diameter of the unsintered PTFE extrudate and the inside surface of the sintering mold is on the order of 2% of the diameter of the sintering mold. The extrudate is drawn into the sintering mold via a plug, inserted into the terminal lumen of the extrudate and a wire and take-up reel. The PTFE extrudate is cut to match the length of the sintering mold, and the sintering mold is sealed on the cut extrudate end. The assembly is transferred to a sintering oven and sintered. During sintering, the extrudate expands in contact with the sintering mold and conforms to the shape of the sintering mold. After cooling, the sintered extrudate contracts away from the sintering mold and assumes an even shape corresponding to the sintering mold.

U.S. Pat. No. 3,196,194 to Ely, Jr., et al., issued Jul. 20, 1965, discloses an extrusion process for making FEP-fluorocarbon tubing. The extrusion process consists of screw-extruding fluid FEP copolymer through a barrel extruder to form a tubular extrudate, placing the tubular extrudate into a heater, pressurizing the tubular extrudate to radially expand the FEP extrudate, and cooling the expanded extrudate to yield a heat shrinkable tube with memory function to the reduced diameter extrudate.

U.S. Pat. No. 4,503,568 to Madras, issued Mar. 12, 1985, discloses an arterial bypass prosthesis for end-to-side anastomosis and reduction of anastomotic hyperplasia. The arterial bypass prosthesis consists generally of a connector element including a tubular entrance member, a tubular exit member and a heel member. The tubular entrance receives and provides an entrance passage for blood flow. The tubular exit member is coupled to and angularly offset from the tubular entrance and provides a passage for the blood from the entrance member. The heel member extends substantially coaxially from the exit member. The distal end of the heel member is inserted through the open arteriotomy and into the portion of the vessel upstream of the arteriotomy. The heel may be solid or may include a passage continuous with the entrance and exist members. A throat portion is located intermediate the tubular entrance and exit members and a circumferential skirt substantially surrounds the throat portion. The skirt heals into the advential tissue of the blood vessel.

With particular reference to known methods for making PTFE materials, the following are cited as examples of the state and scope of the art. U.S. Pat. No. 4,482,516 to Bowman et al., issued Nov. 13, 1984, discloses a process for producing high strength expanded PTFE products having a coarse microstructure. The resulting PTFE microstructure is then defined by a "coarseness" index which purports to consider node size, i.e., height and width and fibril length. U.S. Pat. No. 5,376,110 to Tu et al, issued Dec. 27, 1994, discloses a method of making vascular grafts by collagen cross-linking conducted under the influence of alternating pressure across the graft wall. The alternating pressure aids in cross-linking the collagen fibers. U.S. Pat. No. 4,743,480 to Campbell et al., issued May 10, 1988, discloses a method for extruding and expanding tubular PTFE products in which a helical groove is machined into the extrusion barrel and/or the mandrel. Extrusion of a tubular PTFE product results in an extrudate having nodes angularly displaced between about 85–15 degrees from the longitudinal axis of the extrudate.

Finally, U.S. Pat. No. 4,234,535 to Okita, issued Nov. 18, 1980, discloses a process for forming expanded PTFE vascular grafts having fibers of smaller diameter at the inner surface of the tubing and fibers of at least two times diameter at the outer diameter of the tubing. The grafts are produced by a process in which PTFE tubular extrudates are formed, then placed onto drive and take-up capstans. The capstan drive system conveys the extrudate through a heater set at a temperature above 327° C., then into a vacuum case which causes radial expansion of the extrudate at a temperature above 327° C., then, after radial expansion, the vacuum case is cooled, by introduction of cooled air, to a temperature below sintering temperature, thereby fixing the tube at the expanded diameter and in the longitudinal direction by tension from the drive and take-up capstans. This patent also discloses and claims the use of cooling air conveyed through the tube lumen during the radial expansion process. By conveying cooled air through the tube lumen, the temperature at the lumenal surface is maintained below the PTFE sintering temperature. In this manner, differing fibril diameters at the lumenal and ablumenal surfaces are formed.

In current clinical practice, a peripheral anastomosis between a bypass or access prosthesis and a peripheral artery has been performed by either direct anastomosis, interposition of a venous segment at the anastomotic site, anastomosing the prosthesis with a long venous patch sutured into the artery (Linton Patch), enlargement of the prosthesis within the anastomotic region using a venous patch (Taylor Patch) or interposition of a venous cylinder between the prosthesis and the artery (Miller Collar). In femoro-distal grafting, there is growing evidence that compliance mismatch between the graft and the recipient artery and hemodynamic factors are a major cause of thrombosis and the development of subintimal hyperplasia at the anastomotic site.

BRIEF SUMMARY OF THE INVENTION

It is a principal object of the present invention to provide a new graft for access or femoro-distal bypass grafting made of microporous expanded polytetrafluoroethylene (ePTFE).

It is a further object of the present invention to provide an access or femoro-distal bypass graft made of ePTFE having a distal flange suitable for femoro-crural bypass grafting.

It is a further object of the present invention to provide an access or femoro-distal bypass graft made of ePTFE having a distal flange suitable for arterio-venous patch (AVP) grafting.

It is a further object of the present invention to provide an apparatus and method for making a new graft for access or femoro-distal bypass grafting.

It is a still further object of the present invention to provide an apparatus and method for making a new graft for access or femoro-distal bypass grafting utilizing a tubular mold having a circumferential recess extending radially

from the central axis of the tubular mold to form a distal flange on a tubular polytetrafluoroethylene graft.

These and other objects, features and advantages of the present invention will be more apparent to those skilled in the art from the following more detailed description of the preferred embodiments of invention taken with reference to the accompanying drawings.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. **1** is a diagrammatic representation of peripheral vasculature in a human leg, illustrating an implanted femoro-crural bypass graft.

FIG. **2** is a diagrammatic representation a prior art Miller Collar.

FIG. **3** is a diagrammatic view of a prior art Taylor Patch.

FIG. **4A** is a diagrammatic representation of the inventive graft for hemodialysis access or femoro-crural bypass anastomosed to a peripheral artery.

FIG. **4B** is a perspective view of the inventive graft for hemodialysis access or femoro-crural bypass anastomosed to a section of the peripheral vasculature.

FIG. **5** is a diagrammatic representation of alternative configurations of the inventive graft for hemodialysis access or femoro-crural bypass anastomosed to a peripheral artery.

FIG. **6A** is a diagrammatic representation of the inventive graft for hemodialysis access or AVP bypass.

FIG. **6B** is a perspective view of the inventive graft for hemodialysis access or AVP bypass.

FIG. **7** is a diagrammatic representation of the hemodynamic flow profile through the inventive graft.

FIG. **8** is an exploded elevational view of the inventive apparatus for making the inventive graft.

FIG. **9** is a cross-sectional view taken along lines **9**—**9** of FIG. **8** illustrating a first embodiment of a first mold block for forming the inventive graft.

FIG. **10** is cross-sectional view taken along line **10**—**10** of FIG. **8** illustrating a second embodiment of a first mold block for forming the inventive graft.

FIG. **11** is a cross-sectional view taken along line **11**—**11** of FIG. **8** illustrating a mold tube for forming the inventive graft.

FIG. **12** is a cross-sectional view taken along lines **12**—**12** of FIG. **8** illustrating a second mold block for forming the inventive graft.

FIG. **13** is an elevational view of a second embodiment of the mold for forming the graft in accordance with the present invention.

FIG. **14A** is a longitudinal cross-sectional view illustrating the inventive molding apparatus, a tubular graft within the molding apparatus, and a balloon catheter within the tubular graft prior to radial expansion of the tubular graft within the molding apparatus.

FIG. **14B** is a longitudinal cross-sectional view of the inventive molding apparatus of FIG. **14A**, illustrating the tubular graft after radial expansion within the molding apparatus.

FIG. **15** is a flow diagram illustrating the method for making the inventive femoro-distal bypass graft in accordance with the preferred embodiments of the present invention.

DETAILED DESCRIPTION OF THE INVENTION

FIG. **1** illustrates a sequential femoro-posterior tibial bypass with a PTFE graft to an isolate popliteal segment and a distal graft. The use of a PTFE graft **2** bypassing an occluded section **3** of the femoral artery or an occluded section **4** of the popliteal artery to restore distal circulation is well known. As noted above, various cuff and patch techniques have been devised.

FIG. **2** illustrates a Miller collar **5** in which a venous segment **8**, typically 3–4 cm of the saphenous vein, is obtained and sutured to an open arteriotomy in the popliteal or tibial arteries to form a cylindrical cuff **8** extending outwardly from the artery **2**. The venous segment **8** is fashioned into a collar by opening it longitudinally and anastomosing it to the arteriotomy using a 6/0 or 7/0 prolene suture. The collar is then closed with a 6/0 prolene suture. An ePTFE graft **10** is cut to match the circumference of the collar and then anastomosed to the collar using a continuous 5% prolene suture. The Miller collar **5** is indicated in situations where PTFE is to be anastomosed to tibial arteries, the popliteal artery, or in sequential bypass procedures, e.g., femoro-popliteal-tibial bypass.

FIG. **3** illustrates a Taylor patch **7**. In a Taylor patch **7** procedure, a length of vein 5–6 cm long is harvested, typically from an available segment of saphenous vein. The harvested vein is opened longitudinally and trimmed to form a diamond-shaped vein patch **8**. A distal end of an ePTFE graft **10** is trimmed to a U-shaped open end and a V-shaped slot along an upper surface of the ePTFE graft **10**. The U-shaped open end of the ePTFE graft forms the ePTFE-arterial suture line, while the V-shaped slot is sutured to the venous patch **8**. The vein patch **8** is laid along the V-shaped slot in the ePTFE graft **10** and the open arteriotomy in the correct orientation and sutured to both the ePTFE graft **10** and the arteriotomy. The suture line extends from a heel of the graft to the toe of the graft about the arteriotomy to complete the Taylor patch bypass graft.

Graft patency for standard end-to-side ePTFE graft/arterial anastomoses has been reported between 21 and 60% for one year patency and between 14 and 38% for three year patency. One year patency using the Miller collar has been reported at 47% for ePTFE crural grafts, with three year patency being 52%. One year patency using the Taylor patch has been reported at 86%, with three year patency being reported at 61%. Chester, J. F., et al, "Interposition vein patches for vascular reconstruction," *Hospital Update*, Feb. 1993. Direct PTFE to artery anastomosis has been criticized because of mechanical distortion of the artery by the relatively rigid PTFE and formation of intimal hyperplasia between the PTFE and the recipient artery. These two factors have been implicated in the high occlusion rates and low graft patency characteristic of direct PTFE to artery anastomoses. C. W. Jamison, et al, VASCULAR SURGERY, 330–340 (5th ed. 1994).

The preferred embodiments of the flanged graft are illustrated in FIGS. **4A–6B**. As illustrated in FIG. **4A**, a first embodiment of the flanged graft **10** is a bifurcated double bulb configuration in which an ePTFE tubular graft **11** has a distal bifurcation, forming flanges **12** and **14**. In a distal end-to-side anastomosis the distal end of the graft **11** is anastomosed to an open arteriotomy formed in the wall of a receiving artery **2**. The bifurcated flanges **12** and **14** project in opposing directions substantially perpendicular to the central longitudinal axis of the graft **11** to facilitate the anastomosis, increase compliance matching between the ePTFE graft **11** and the receiving artery **2**, and to optimize hemodynamic flow from the graft **11** into the receiving artery **2**. When the graft **11** is positioned in an end-to-side relationship with the receiving artery **2**, each of the bifurcated flanges **12** and **14** lie substantially parallel to the

longitudinal axis of the receiving artery **2** and extend in the proximal and distal directions relative to the receiving artery **2**. The bifurcated flanges **12** and **14** preferably have an elongated bulbous configuration which permits the bifurcated flanges **12** and **14** to be circumferentially positioned substantially co-incident with the curvature of the receiving artery **2** and subtending the open arteriotomy (not shown). Bifurcated flanges **12** and **14** are each preferably formed to have a substantially elliptical shape with outer arcuate peripheral edges **20** and **18** terminating in toe portions **21** and **19** respectively. A heel region **17** is immediately contiguous with the tubular graft **11** and each of the arcuate peripheral edges **20** and **18** of bifurcated flanges **12** and **14**. The juncture between the peripheral edge **20** of flange **12** and the peripheral edge **18** of flange **14** at the heel region **17** form a crotch angle **16**. Crotch angle **16** is preferably between 45 and 180° to maximize the strength of the graft at heel region **17**.

The bifurcated flanges **12** and **14** may be symmetrical or asymmetrical relative to one another. The selection of symmetrical or asymmetrical bifurcated flanges **12** and **14** is preferably determined by the vascular surgeon based upon the identity of the receiving artery **2**, the position of the arteriotomy on the receiving artery **2** and the lumenal diameter of the graft **11**. The graft **11** is preferably anastomosed to the receiving artery **2** using continuous sutures **22** to join the arteriotomy to the peripheral edges **20** and **18** of the bifurcated flanges **12** and **14**, the heel region **17** and the crotch angle **16**. FIG. **4B** depicts a perspective view of the first embodiment of the graft **10** anastomosed to a receiving artery **2**.

FIG. **5** illustrates various sizes and symmetries of the bifurcated flanges at the distal end of a tubular ePTFE graft **11** anastomosed to a receiving artery **2**. A first graft has asymmetrical bifurcated flanges **30, 40** in which flange **30** has a greater surface area than flange **40**, with flange **30** extending laterally from and circumferentially about the graft **11** a greater extent than flange **40**. The crotch angle **41** of the first graft is offset toward the shorter flange **40** relative to the median line **31** of the graft **11**. The configuration of the first graft having flanges **30, 40** is well suited to end-to-side anastomoses where the angular orientation between the graft **11** and the receiving artery **2** is oblique on the side of the shorter flange **40** and obtuse on the side of the longer flange **30**.

A second graft has substantially symmetrical bifurcated flanges **34, 36**, with the crotch angle **37** being substantially co-incident with the median line **31** of the graft **11**. Both of flanges **34** and **36** extend substantially identical lengths laterally and in opposite directions relative to the graft **11** and the arcuate peripheral edges of the flanges **34, 36** extend circumferentially about the receiving artery **2** to a substantially equivalent extent. The second graft with symmetrical bifurcated flanges **34, 36** is particularly useful where the angular orientation of the end-to-side anastomosis between the graft **11** and the receiving artery **2** is substantially perpendicular.

The third graft, denoted by asymmetrical bifurcated flanges **38, 32**, is substantially a mirror image of the first graft, denoted by asymmetrical bifurcated flanges **30, 40**. In this third graft, the flange **32** projects laterally from and extends circumferentially about the graft **11** a greater extent than flange **38**. The crotch angle **33** of the third graft is offset toward the shorter flange **38** relative to the median line **31** of the graft **11**. The configuration of the third graft, having flanges **38, 32** is well suited to end-to-side anastomoses where the angular orientation between the graft **11** and the receiving artery **2** is acute on the side of the shorter flange **38** and obtuse on the side of the longer flange **32**.

In each of the three preferred embodiments of the bifurcated flange graft **10**, the bifurcated flanges are preferably made of ePTFE and formed as a continuous, integral, monolithic section of the ePTEE tubular graft **11**, without intervening seams or overlap regions.

From the foregoing, those skilled in the art will understand that the use of asymmetrical bifurcated flanges on the flanged graft **10** is particularly well suited to end-to-side anastomoses where the longitudinal axis of the inflow graft is positioned at an acute angle relative to the receiving artery **2**, with the longer flange being distally-oriented and the shorter flange being proximally oriented relative to the direction of blood flow.

Dimensionally, it is preferable to fabricate each bifurcated flange to a length which is between 1 to 5 times the lumenal diameter of the graft. Thus, for a 5 mm graft, the shorter flange should be no less than 5 mm in length measured from the outer surface of the graft to the furthest point on the toe region of the flange, and the longer flange should be no greater than 25 mm, measured from the outer surface of the graft to the furthest point on the toe region of the flange. Circumferentially, each bifurcated flange should extend no greater than 1 times the lumen diameter of the graft about the receiving artery. Thus, where a graft has a lumenal diameter of 5 mm, the bifurcated flange should extend no further than 5 mm measured from the median line of the graft to a point on the arcuate peripheral edge of the flange which is circumferentially furthest from the median line of the graft. These dimensional constraints have been found to represent optimal parameters for an ePTFE femoro-infragenicular bypass graft which does not use a venous patch or collar at the ePTFE-arterial junction. The configuration of bifurcated flanged graft **10** has been found to have an optimal geometry and a reduced probability of developing subintimal hyperplasia as a cause of graft failure. The inventive bifurcated flanged graft **10** has shown minimal presence of zones of low flow velocity or vortex formation at the anastomotic site and exhibits an optimal hemodynamic flow pattern for an end-to-side anastomosis.

Conventional end-to-side anastomoses exhibit complex hemodynamic flow patterns at the anastomotic junction. Zones of low flow velocity, reversed flow velocity and vortex formation are found in virtually all types of known end-to-side anastomoses. Clearly, detailed hemodynamic measurements are difficult to obtain in vivo. A pulsatile flow model was developed to simulate hemodynamic conditions within the distal end-to-side anastomosis of the inventive femoro-infragenicular bypass graft **10**. A closed flow loop system was made by connecting two reservoirs maintained at systolic and diastolic pressure. A magnetic valve was used to generate a pulsatile flow representative of that in the femoral arteries. A blood-analog fluid (7.5% Dextran by weight in distilled water) was used. To enhance sonographic visualization, the blood-analog fluid was seeded (1 g/L) with 40–120 m SEPHADEX particles (Pharmacia, Uppsala, Sweden). Flow visualization and velocity field measurements were accomplished by direct dye injection and Doppler color flowometry using real-time ultrasonography (Acuson 128 XP/10) with a 5 MHZ linear array transducer having a Doppler frequency of 3.5 MHZ and an aperture size of 3.8 cm. Doppler color flowometry images were continuously recorded using an S-VHS video camera and an S-VHS high resolution video cassette recorder. Images were obtained at specific intervals within the pulsatile cycle using a peak capture techniques which map peak velocities at each

pixel in the frame during successive one second intervals. Flow velocity measurements were detected using ultrasound beams transmitted at an angle of 70° to the face of the transducer in an upstream or downstream direction.

The bifurcated flanged graft **10** was tested against the Linton patch and the Taylor patch using the dye injection and Doppler color flowometry flow visualization techniques under both low and high pulsatile flow rates. In both the Linton patch and the Taylor patch, the velocity profile was skewed toward the outer wall of each graft, independent of flow rates. An impingement of the flow stream on the outer wall produced circumferential flow motions in the high flow situation, while under low flow conditions, a region of flow stagnation was identified at the host vessel outer wall and in line with the inner wall of the graft. This point marked a flow split zone where one flow stream moved in the distal branch and one flow stream moved in the proximal branch of the recipient artery. In the inventive bifurcated flanged graft **10**, the area of flow splitting was virtually eliminated. Flow vortexing was observed in the toe and heel regions of the Taylor patch and Linton patch was observed. Minimal vortex formation was observed at the anastomotic site of the inventive bifurcated flanged graft **10**. The flow profile through the inventive bifurcated flanged graft **10** is depicted in FIG. **7**.

Under Doppler color flowometry, both the Linton patch and the Taylor patch produced the following hemodynamic profiles: 1) flow splitting into reversed vortex flow in the upstream and forward flow in the downstream direction, 2) flow jetting and a non-homogeneous flow pattern downstream of the anastomotic site, and 3) low flow regions with zero flow or reverse flow. The primary location for each of these hemodynamic phenomenon were opposite to the graft inlet and along the inner wall of the artery from the toe of the anastomosis to downstream. Variation of flow patterns with deceleration of flow waveform from systole to diastole resulted in and increase of low flow regions in both the Linton patch and the Taylor patch. None of these hemodynamic phenomena were observed with any degree of statistical significance with the inventive bifurcated flanged graft **10**, which exhibited a substantially laminar flow pattern illustrated in FIG. **7**.

In a clinical study, 65 infragenicular bypass grafts using the inventive bifurcated flanged graft **10** were performed on 62 patients. In 18 of the patients, a temporary extracorporeal bypass was inserted between the proximal and distal anastomotic sites for measurement of blood flow and pressure to calculate the peripheral arterial resistance in each of the upstream and downstream directions. Patency of the inventive grafts was tracked. Prior to the bypass operation, all patients underwent Doppler ultrasonographic ankle artery pressure measurements and arteriography. Graft patency was tracked by clinical examination and Doppler ultrasonographic arterial pressure studies on all patients at three month intervals. The morphology of the anastomosis was examined postoperatively by angiography and at each three month interval with Doppler color flowometry. The one year primary patency rate was 60% which remained constant over the second year of follow up. The one year secondary patency rate was 68% while the second year patency rate fell only to 60%.

Turning now to FIGS. **6**A and **6**B, there is shown a second preferred embodiment of the bypass graft, referred to for purposes of identification as the arterio-venous patch (AVP) prosthesis **50**. The AVP prosthesis **50** consists generally of a tubular ePTFE graft member **52** which has an outwardly flared skirt **56** which extends circumferentially about the tubular ePTFE graft member **52**. The flared skirt **56** preferably has a generally elliptical shape and is offset from a central longitudinal axis **53** of the tubular ePTFE graft member **52**, such that one focal point of the elliptically shape flared skirt **56** is positioned a greater distance from the central longitudinal axis **53** of the tubular ePTFE graft member **52** than another focal point of the elliptically shaped flared skirt **56**. Additionally, the flared skirt **56** resides in a plane **55** which is distally and angularly offset relative to the central longitudinal axis **53** of the tubular ePTFE graft member **52**. By being distally and angularly offset relative to the central longitudinal axis **53** of the tubular ePTFE graft member **52**, the flared skirt **56** forms a toe angle **62** and a heel angle **60** with the tubular ePTFE graft member **52**. In accordance with the preferred embodiments of the AVP prosthesis **50**, the toe angle **62** is greater than 90° relative to the central longitudinal axis **53** of the tubular graft member **52**, while the heel angle **60** is less than 90° relative to the central longitudinal axis **53** of the tubular graft member **52**. In accordance with the preferred embodiments of the present invention, it is preferable that the toe angle **62** be within the range of 95° to 160° relative to the central longitudinal axis **53** of the ePTFE tubular graft member **52**, while the heel angle **60** be within the range of 20° to 85° relative to the central longitudinal axis **53** of the ePTFE tubular graft member **52**.

Flared skirt **56** has a toe section **67** which projects outwardly from the ePTFE tubular member **52** at toe angle **62**. The length of toe section **67** may be predetermined during manufacture, or may be trimmed by a vascular surgeon during the implant procedure to accommodate the open arteriotomy at the anastomotic site. A heel section **69** projects outwardly from the ePTFE tubular member **52** at heel angle **60**, and in an opposing direction from the toe section **67**. A curved outer peripheral edge **58** of the flared skirt **56** subtends a 180° arc and forms a continuous surface interconnecting toe section **67** and heel section **69**. Depending upon the desired length of toe section **67**, the length of curved outer peripheral edge **58** and the extension distance **71** which the flared skirt **56** projects in the distal direction relative to the ePTFE tubular member **52** will vary. Phantom lines **64** and **66** depict alternative curved outer peripheral edges **64** and **66** of the flared skirt **56**.

The flared skirt **56** is preferably made of ePTFE and is formed as a continuous, integral, monolithic part of the ePTFE tubular graft member **52**, without any intervening seam or overlap. As illustrated in FIG. **6**B, the flared skirt **56** assumes a curved configuration in its z-axis to enable a suture anastomosis between the outer peripheral edge **58** and about a circumferential aspect of an artery. The flared skirt **56** should, preferably, extend a distance no greater than the lumenal diameter of the ePTFE tubular graft member **52**, measured from an upper surface of the toe region **67** to a point along the outer peripheral edge **58** of the flared skirt **56** which is furthest from the upper surface of the toe region **67**.

In accordance with the preferred embodiments of the AVP prosthesis **50**, the toe region **67** will have a length greater than that of the heel region **69**, with the toe region **67** projecting outwardly from the central longitudinal axis **53** of the tubular ePTFE graft member **52** in the direction of the blood flow. As noted above, the length of toe region **67** is variable, preferably within the range of 5 to 25 mm measured from an outer wall surface of the ePTFE tubular graft member **52** adjacent the toe region **67**, to a furthest point on the outer peripheral edge **58** of the toe region **67**. It has been found preferable, however, to maintain the length of heel region **69** to a fixed length of approximately 3 mm, mea-

sured from the outer wall surface of the ePTFE tubular graft member **52** adjacent the heel region **69**, for femoro-distal bypass anastomoses.

The foregoing preferred embodiments of the flanged bypass grafts **10** and **50** may be made by the following described inventive method using the following described inventive apparatus for making the flanged bypass grafts **10** and **50**. FIGS. **8–13** depict alternative embodiments of molding apparatus **100** and **130** which are preferably used in accordance with the method depicted in the flow diagram at FIG. **15**.

With particular reference to FIGS. **8–12**, there is depicted a molding apparatus **100** for making the flanged bypass grafts **10** and **50**. Molding apparatus **100** consists generally of molding tube **102** having a lumenal cavity **101** which extends through an entire longitudinal length of the molding tube **102** and opens to each of two opposing ends of the molding tube **102**. Molding tube **102** further includes a plurality of apertures **112** passing through a portion of a hemispherical cross-section of the molding tube **102**. The plurality of apertures **112** are positioned in a linear array extending along a longitudinal axis of the molding tube **102** and positioned at each opposing end of the molding tube **102**.

A first block member **104** and a second block member **106**, each having a tubular shape and an outer diameter configured to be reciprocally engageable within the lumenal cavity **101** of molding tube **102**, are provided. First block member **104** has a longitudinally oriented lumen **105** which extends through an entire longitudinal length of first block member **104** and is open at each of two ends of the first block member **104**. First block member **104** has a planar face **108** which is oriented non-perpendicular relative to the longitudinal axis of the first block member **104**. A plurality of apertures **112** extend through the first block member **104** and are positioned as a longitudinal array with each aperture **112** positioned to positionally correspond to the apertures **112** in the molding tube **102**. The plurality of apertures **112** in the first block member pass laterally through the first block member **104** intermediate between the longitudinally oriented lumen **105** and an outer diameter of the first block member **104**.

Like first block member **104**, second block member **106** has a longitudinally oriented lumen **107**, which extends through an entire longitudinal length of the second block member **106**, is open at each of two ends of the second block member **106** and is co-axial with the lumen **105** of the first block member **104**. Second block member **106** has a planar face **110** which is oriented non-perpendicular relative to the longitudinal axis of the second block member **106** and is substantially parallel to planar face **108** of the first block member **104**. A plurality of apertures **112** extend through the second block member **106** and are positioned as a longitudinal array with each aperture **112** situated to positionally correspond to at least some of the apertures **112** in the molding tube **102**. The plurality of apertures **112** in the second block member **106** pass laterally through the second block member **106** intermediate between the longitudinally oriented lumen **107** and an outer diameter of the second block member **106**.

The molding apparatus **100** is assembled by engaging the first block member **104** within the lumen **101** of the molding tube **102** by inserting the first block member into a first open end of the molding tube **102**, aligning at least one of the plurality of apertures **112** in the first block member **104**, with at least one of the plurality of apertures **112** in the molding tube **102** and inserting a lock pin **113** into the aligned at least one of a plurality of apertures **112** such that it engages both the molding tube **102** and the first block member **104** in a fixed position relative to one another. The second block member **106** is then engaged within the lumen **101** of the molding tube **102** by inserting the second block member into a second open end of the molding tube **102**, aligning at least one of the plurality of apertures **112** in the second block member **106**, with at least one of the plurality of apertures **112** in the molding tube **102** and inserting a lock pin **113** into the aligned at least one of a plurality of apertures **112** such that it engages both the molding tube **102** and the second block member **106** in a fixed position relative to one another, and the planar faces **108** and **110** of the first block member **104** and the second block member **106** are substantially parallel to one another and in a spaced apart relationship relative to one another defining a molding space **120** therebetween. By providing planar faces **108** and **110** oriented at a desired angle relative to the longitudinal axis of the first **104** and second **106** block members, and parallel to one another, the molding space **120** defined therebetween is bounded by the parallel, angularly displaced faces **108** and **110** and sections of the lumenal wall of the molding cavity **101** and has a generally trapezoidal cross-sectional shape. The depiction of molding tube **102** in FIG. **8** illustrates one embodiment of the molding apparatus **100** in its assembled state by phantom lines.

Also shown in FIG. **8** are alternative embodiments **104'** and **106'** of the first block member **104** and the second block member **106**, respectively. The first alternative embodiment of the second block member **106'** is a stepped-diameter lumen first block member **114** in which the longitudinally oriented lumen has a first diameter **116** and a second diameter **117** at different positions along the lumen. By providing a stepped-diameter lumen **115**, it is possible to create a taper in the resulting graft proximal to the flange or skirt which is formed within the molding space **120**, as will be described in greater detail hereinafter. The second alternative embodiment of the first block member **104'** and second block member **106'** is virtually identical to the first block member **104** and second block member **106**, except that planar faces **124** and **128** are oriented substantially perpendicular to the longitudinal axis of the first block member **104'** and the second block member **106'**. By providing planar faces **124**, **128** oriented substantially perpendicular to the longitudinal axis of each of the first **104'** and second **106'** block members, the molding space **120** formed therebetween is bound by the perpendicular planar faces **124**, **128**, and the lumenal diameter of the molding cavity **101** and has a generally rectangular or quadrilinear cross-sectional shape. Any of the first **104** or the second **106** block members, or their alternative embodiments **104'** or **106'**, may include a stepped lumen **105**, **107** respectively, as illustrated in connection with the foregoing description of the first alternate embodiment **114** of the second block member. Further, the angular orientation of the face **110** or **124** may be selected as desired depending upon the resulting angular displacement desired for the flange or cuff on the flanged graft made by the inventive apparatus.

FIGS. **9–12** are cross-sectional views of sections of the apparatus for making the inventive flanged bypass graft. FIG. **9** is a cross-sectional view taken through the second block member **106**, illustrating the body of the second block member **106**, the longitudinally oriented lumen **107** and one of the plurality of apertures **112** passing laterally through the second block member **106**. FIG. **10** is a cross-sectional view of the stepped-diameter lumen second block member **114**

taken along line 10—10 of FIG. 8. The body of the first block member 114 shown with the central longitudinal lumen 115 passing therethrough, and showing the first lumenal diameter 116, the second lumenal diameter 117 and one of the plurality of apertures 112 passing laterally through the stepped-diameter lumen second block member 114. FIG. 11 is a cross-sectional view of the molding tube 102, taken along line 11—11 of FIG. 8. In FIG. 11, it is seen that aperture 112 passes laterally through the molding tube 102 and opens into the lumen 101 of the molding tube 102 to facilitate alignment with the apertures 112 in the first block member 104, the second block member 106 or the stepped-diameter second block member 114, upon engagement with the molding tube 102, to receive lock pin 113 therethrough. Finally, FIG. 12 is a cross-sectional view taken along lines 12—12 in FIG. 8 and illustrate the body of the first block member 104, the central longitudinal lumen 105 and one of the apertures 112 passing laterally through the body of the first block member 104 without impinging into lumen 105.

It will be understood, by those skilled in the art, that when the molding tube 102, the first block member 104 and the second block member 106 are assembled and secured with a plurality of lock pins 113 inserted into apertures 112, lumen 105 of the first block member 104, and co-axial lumen 107 of the second block member 106, form a common longitudinal lumen 122 which passes through the entire longitudinal axis of the molding apparatus 100 and is open to the two opposing ends of molding tube 102 and to the molding cavity 120. Common longitudinal lumen 122, therefore, affords bilateral access to the molding cavity 120. As will be described in greater detail hereinafter, an expanded polytetrafluoroethylene tubular graft is axially passed into the common longitudinal lumen 122, past the molding cavity 120 so that a longitudinal portion of the ePTFE tubular graft resides in the molding cavity 120. A radially expansive force is then applied to the longitudinal portion of the ePTFE tubular graft resident within the molding cavity 120 which radially expands the longitudinal portion of the ePTFE tubular graft material resident within the molding cavity 120, thereby forming the flange or skirt section of the inventive distal bypass graft. The radially expansive force may be applied either through the graft lumen or external to an outer wall surface section of the longitudinal portion of the ePTFE tubular graft or created by a pressure differential applied across the longitudinal portion of the ePTFE tubular graft within the molding cavity 120.

FIG. 13 depicts a second preferred embodiment of a molding apparatus 130 in accordance with the present invention. As distinguished from the molding apparatus 100 depicted in FIGS. 8–12, the molding apparatus 130 is assembled as a unitary non-adjustable apparatus. Molding apparatus 130 consists of a molding tube 132 having a molding cavity 134, which may be configured in any manner desired to produce a skirt of a flange. The molding cavity 134 may be oriented at a non-perpendicular angle relative to the longitudinal axis of the molding apparatus 130, assuming a trapezoidal longitudinal cross-sectional profile, as depicted in FIG. 13 or perpendicular relative to the longitudinal axis of the molding apparatus 130, assuming a generally rectangular longitudinal cross-sectional profile (not shown). The molding cavity 134 may further be dimensioned such that the volume of mold cavity 134 is selected based upon the size and shape of skirt or flange desired in the resulting flanged distal bypass graft produced in molding apparatus 130. Molding tube 132 further includes opposing laterally projecting port members 133, 135, each having a lumen 138, 137, respectively, which are co-axial relative to one another. Optionally, lumen 138 of port member 133 may have a tapered section 140 which transitions between a diametrically larger or smaller lumen 138. Tapered section 140 of lumen 138 permits a corresponding tapered region to be formed either proximal or distal to the flange or skirt in the inventive flanged distal bypass graft.

Both molding apparatus 100 and 130 are preferably made of either a polymer plastic or metal capable of withstanding pressures up to 100 psi without substantial dimensional distortion. It is further preferable, though not required by the present invention, that both the molding apparatus 100 and 130 also be made of a high temperature material capable of being exposed to temperatures in excess of at least the crystalline melt point temperature of polytetrafluoroethylene, i.e., 327° C., and preferably up to and including 450° C., without substantial dimensional distortion.

A wide variety of methods may be used to apply a radially expansive force to the longitudinal section of ePTFE resident within the molding apparatus 100 and 130, particularly the longitudinal section of ePTFE resident within the molding cavities 120 and 134. In accordance with the best mode contemplated for the invention, a compliant angioplasty balloon catheter has been used to apply a radially expansive force to the ePTFE tubular graft material within the molding apparatus 100 and 130. A sintered ePTFE tubular graft was engaged into and through the common longitudinal lumen 122 of a fully assembled molding apparatus 100. An angioplasty balloon catheter was passed though the lumen of the sintered ePTFE tubular graft until the balloon was positioned within a longitudinal section of the ePTFE graft which resides in the molding cavity 120. The angioplasty balloon was inflated by applying a positive pressure to a body of water from a pressure syringe, through the catheter lumen to the angioplasty balloon. Radial expansion of the angioplasty balloon caused the balloon to impinge upon the lumenal wall of the ePTFE tubular graft, which then radially expanded by deformation of the polytetrafluoroethylene material matrix under the influence of the applied radial pressure into the molding cavity 120. After radial expansion of the ePTFE tubular graft was completed, the radially expansive fluid pressure was withdrawn, the balloon collapsed and the angioplasty balloon catheter removed from the lumen of the ePTFE tubular graft. The ePTFE tubular graft was then removed, and trimmed to form a bilateral flange as described above with reference to the preferred embodiment of the flanged distal bypass graft 10.

Alternative methods of radially expanding an ePTFE tubular graft within the molding apparatus 100 or 130 are also contemplated by the present invention. Other such alternative methods include, without limitation:

a) using a non-compliant shaped balloon where the shape of the non-compliant balloon corresponds to the shape of the molding cavity 120, 134;

b) employing an expansion mandrel having a radially expanding member coupled to the expansion mandrel;

c) using a spider member in which a section of the spider member circumferentially extends from a central rod member under the influence of an applied positive pressure and impinges upon a lumenal surface of the ePTFE graft to radially expand the ePTFE graft into the molding cavity 120, 134;

d) employing a coil spring member in which a coil spring section of a longitudinal rod member uncoils under upon torsional rotation of the longitudinal rod member

and impinges upon a lumenal surface of the ePTFE graft to radially expand the ePTFE graft into the molding cavity **120**, **134**; or

e) utilizing a mesh spring member, fixed on a distal end to a first rod member and fixed on a proximal end to a second rod member, concentric and co-axial with the first rod such that axial movement of the first rod and second rod members relative to one another longitudinally compresses or longitudinally extends the mesh spring member, causing the mesh spring member to extend radially from the first and second rod members upon a compression stroke, and return to a concentric, non-radially extended position upon an axial extension stroke.

FIGS. **14**A and **14**B illustrate the inventive molding apparatus **100** having an internal mold cavity **120**, with an ePTFE tubular graft **142** axially positioned in the molding apparatus **100** before (FIG. **14**A) and after (FIG. **14**B) radial expansion within the mold cavity **120**. A balloon catheter **144** having a radially expandable balloon **146**, which is either a compliant balloon which substantially assumes the dimensional configuration of the mold cavity **120** upon expansion or is a non-compliant balloon to correspond to the dimensional configuration of the mold cavity **120**, is axially positioned with the lumen of the ePTFE tubular graft **142** such that the balloon **146** is adjacent a longitudinal section of the ePTFE graft **142**, which is resident in the mold cavity **120**. Inflation of the balloon catheter **144**, using a positive fluid pressure, typically provided by a syringe pump and water or saline, radially expands the balloon **146** into contact with the lumenal surface of the ePTFE tubular graft **142** and, upon application of sufficient pressure, the longitudinal section of the ePTFE tubular graft **142** resident within the mold cavity **120** is radially expanded and urged into conformation with the dimensional configuration of the mold cavity **120** as shown in FIG. **14**B. It has been found that the pressure required to radially expand the longitudinal section of the ePTFE tubular graft **142** within the mold cavity **120** is dependent upon the material properties of the ePTFE tubular graft selected. The material properties of the ePTFE which govern radial expansion pressures include, without limitation, wall thickness, porosity, internodal distance, burst strength, radial tensile strength, and hoop stress. Experiments conducted using the molding apparatus **100** and an embolectomy balloon catheter have found that the applied pressures to radially expand a longitudinal section of an ePTFE tubular graft into the mold cavity **120** range from approximately 26 psi to about 100 psi at approximately 37° C. to radially expand ePTFE tubular grafts having wall thicknesses of 0.3 to 0.6 mm by between approximately 25% to about 500% the original diameter of the ePTFE tube.

The method **150** for making the flanged distal bypass graft using the inventive molding apparatus **100**, **130** is described in the flowchart presented in FIG. **15**. A mold with a predetermined mold cavity configuration corresponding to the taper, flange, or skirt configuration desired is provided at step **152**. The mold may be a pre-assembled mold or may be assembled at step **154** from a molding tube and mold blocks as described above. An ePTFE tubular graft is then loaded onto a loading mandrel in step **156**, the loading mandrel having an outer diameter which permits the selected ePTFE tubular graft to be loaded concentrically thereupon with a tight tolerance between the loading mandrel and the ePTFE graft without substantially radially expanding the graft on the loading mandrel. Alternatively, the loading mandrel may have an outer diameter which is larger than the inner diameter of the ePTFE tubular graft by up to 30% in order to pre-dilate the ePTFE tubular graft and lower the applied pressure needed to radially expand the ePTFE tubular graft into the mold cavity. Furthermore, the loading mandrel may have a tapered section which positionally corresponds to a tapered lumenal section of the molding apparatus to further facilitate radial expansion of the ePTFE tubular graft in the molding apparatus.

The loading mandrel with the ePTFE tubular graft mounted thereupon is then axially positioned in the molding apparatus in step **158** and the loading mandrel is withdrawn in step **160**. A radially expansive pressure is exerted to the ePTFE tubular graft in step **162** to radially expand at least a longitudinal portion of the ePTFE tubular graft into the mold cavity of the molding apparatus in step **170**. As described above, the radially expansive pressure may be an applied fluid pressure at step **164**, a mechanically deforming mandrel, such as a spider, a radially expansive mesh, or the like, at step **166**, or a compliant or shaped non-compliant balloon, such as an angioplasty or embolectomy balloon catheter at step **168**. The radially expansive force is then released at step **172**, and the molded graft is withdrawn from the mold and trimmed by cutting or other means to obtain the desired shape of flange or skirt at step **174**.

While the foregoing is a description of the broad method steps of the inventive method **150**, it is believed within the ordinary skill of one in the art to define the particular mold configuration, the means for exerting a radially expansive pressure to the ePTFE tubular graft, the desired material properties of the ePTFE tubular graft, and temperatures and pressures under which the method is executed. Thus, while the present invention has been disclosed and described with reference to its preferred embodiments, those skilled in the art will understand and appreciate that modifications in material selection, dimension, and construction may be made without departing from the scope of the present invention, which is limited only by the claims appended hereto.

What is claimed is:

1. A method for making a vascular graft, comprising the steps of:

radially expanding at least a longitudinal section of a tubular graft member formed of microporous expanded polytetrafluoroethylene in a mold cavity to an expanded diameter which is greater than remaining radially unexpanded longitudinal sections of the expanded polytetrafluoroethylene tubular graft member, where a tapered longitudinal section is interdisposed between the radially expanded and radially unexpanded longitudinal sections of the expanded polytetrafluoroethylene tubular graft member;

removing the expanded polytetrafluoroethylene tubular graft member from the mold cavity; and

trimming the expanded polytetrafluoroethylene tubular graft member to form a vascular graft having at least one flanged section or a collar section projecting from a distal end thereof.

2. The method of claim **1**, wherein the step of trimming comprises forming at least one flanged section which projects outwardly away from a central axis of the tubular graft member at the distal end thereof, the at least one flanged section being a continuous and integral section of the expanded polytetrafluoroethylene tubular graft member.

3. The method of claim **2**, wherein the step of trimming further comprises a step of forming a collar section circumferentially extending about an entire circumferential aspect of a distal end of the radially expanded longitudinal section of the expanded polytetrafluoroethylene tubular graft member.

4. The method of claim 2, wherein the step of trimming further comprises forming a collar section as an elliptical shape having foci offset with respect to a central longitudinal axis of the expanded polytetrafluoroethylene tubular graft member and angularly displaced such that a greater aspect of the elliptical shape projects distally and a smaller aspect of the elliptical shape projects proximally relative to the longitudinal axis of the expanded polytetrafluoroethylene tubular graft member.

5. The method of claim 1, wherein the step of trimming comprises forming at least one flanged section projecting radially outwardly away from a central axis of the tubular graft member.

6. The method of claim 5, wherein the step of trimming comprises forming at least one flanged section, and the step of forming at least one flanged section further comprises the step of forming two flange sections projecting radially outward from the central axis of the tubular graft member and in opposing directions relative to one another.

7. The method of claim 6, wherein the two flange sections as substantially symmetrical mirror-images of one another.

8. The method of claim 6, wherein the two flange sections as substantially asymmetrical to one another.

9. The method of claim 1, wherein the step of trimming comprises forming a collar section circumferentially extending about an entire circumferential aspect of the distal end of the radially expanded longitudinal section of the expanded polytetrafluoroethylene tubular graft member.

10. The method of claim 9, wherein the collar section is formed as an elliptical shape having foci offset with respect to a central longitudinal axis of the expanded polytetrafluoroethylene tubular graft member and angularly displaced such that a greater aspect of the elliptical shape projects distally and a smaller aspect of the elliptical shape projects proximally relative to the longitudinal axis of the expanded polytetrafluoroethylene tubular graft member.

11. The method of claim 10, wherein the step of forming the collar section further comprises forming a toe section and a heel section, the toe section comprising the greater aspect of the elliptical shape and the heel section comprising the smaller aspect of the elliptical shape.

12. The method of claim 11, wherein the step of forming the collar section further comprises the step of molding the toe section such that it is angularly displaced between 95° to 160° relative to a central longitudinal axis of the expanded polytetrafluoroethylene tubular graft member.

13. The method of claim 12, wherein the step of forming the collar section further comprises the step of molding the heel section such that it is angularly displaced between 20° to 85° relative to the central longitudinal axis of the expanded polytetrafluoroethylene tubular graft member.

14. The method of claim 13, wherein the step of forming the collar section further comprises the step of trimming an arcuate outer peripheral edge which subtends an arc of 180° arc and forms a continuous surface interconnecting the toe section and the heel section.

15. An apparatus for making a flanged vascular graft, comprising:

a molding tube member having first and second open ends;

a first tubular mold block member having a central longitudinally oriented lumen and a mold face, the first tubular mold block being engageable within the molding tube member at the first open end thereof,

a second tubular mold block member having a central longitudinally oriented lumen and a mold face, the second tubular mold block being engageable within the molding tube member at the second open end thereof,

a common lumen defined by the each of the central longitudinally oriented lumens of the first and second tubular mold block members which are co-axially aligned relative to one another, the common lumen communicating between the first and second open ends of the molding tube member;

a mold cavity defined by the mold faces of each of the first and second tubular mold block members and a circumferential section of the molding tube member; and

means for retaining the first and second mold block members in a fixed position within the molding tube member comprising a plurality of apertures passing through each of the molding tube member, the first mold block member and the second mold block member, wherein said plurality of apertures are capable of variable alignment with one another, and a plurality of lock pin members engageable through the plurality of apertures.

16. The apparatus of claim 15, wherein at least one of the lumen of the first mold block member and the lumen of the second block member further includes a tapered section transitioning between a larger lumenal diameter and a smaller lumenal diameter section of the lumen.

17. The apparatus of claim 15, wherein at least one of the lumen of the first mold block member and the lumen of the second block member further includes a tapered section transitioning between a larger lumenal diameter and a smaller lumenal diameter section of the lumen.

18. The apparatus of claim 15, wherein the means for retaining the first and second mold block members further comprises an adhesive.

19. The apparatus of claim 18, wherein at least one of the lumen of the first mold block member and the lumen of the second block member further includes a tapered section transitioning between a larger lumenal diameter and a smaller lumenal diameter section of the lumen.

* * * * *

UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE OF CORRECTION

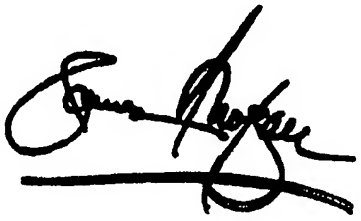
PATENT NO. : 6,190,590 B1
DATED : February 20, 2001
INVENTOR(S) : Scott Randall, Roy H. Tang and Albert L. Lamay

It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

Column 17,
Line 21, change "as" to -- are --.
Line 23, change "as" to -- are --.

Signed and Sealed this

Eleventh Day of June, 2002



Attest:

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JAMES E. ROGAN
Director of the United States Patent and Trademark Office